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CONTENTS OF PREVIOUS NUMBER

JULY 1947. NUMBER 1

Copper Sulfate Method for Rapid Estimation of Whole Blood Requirements. Joseph C. Edwards, M.D., St. Louis.

Total Gastrectomy. Henry K. Ransom, M.D., Ann Arbor, Mich.

Recent Advances in Vascular Surgery: A Review of the Literature. Ralph A. Deterling Jr., M.D., Rochester, Minn.

Osteotomy in Treatment of Fractures of the Hip. Elsie Asbury, M.D., Cincinnati.

Treatment of Localized Infections with Penicillin Infiltration. Frank K. Inui, M.D., Columbus, Ohio.

Progress in Orthopedic Surgery for 1945. A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons:

XIX. Conditions Involving the Elbow, the Forearm, the Wrist and the Hand. Walter C. Graham, M.D., Santa Barbara, Calif.

XX. Conditions Involving the Spine and Thorax, Exclusive of Those in the Lower Part of the Back. John R. Cobb, M.D., New York.

XXI. Conditions Involving the Lower Part of the Back. R. Beverly Raney, M.D., Durham, N. C.

ARCHIVES OF SURGERY

VOLUME 55 AUGUST 1947 NUMBER 2

COPYRIGHT, 1947, BY THE AMERICAN MEDICAL ASSOCIATION

MECHANISM OF ACUTE ABDOMINAL DISTENTION

Some Observations

CHARLES R. MORRIS, M.D.
Fellow in Surgery, Mayo Clinic
ROCHESTER, MINN.
AND
ANDREW C. IVY, Ph.D., M.D.
AND
WALTER G. MADDOCK, M.D.
CHICAGO

INTRODUCTION

THE STIMULUS for this study evolved in part from an unusual case of acute, massive pneumoperitoneum occurring in a child after perforation of an ileal ulcer opposite the neck of a Meckel diverticulum.[1] The extreme abdominal distention with encroachment on the thorax, as shown in figure 1, was deflated by paracentesis, and yet at the time of the operation, less than one hour later, the distention had returned to its original size and the respiratory rate had increased to 45 per minute.

Where did such a large volume of gas come from and how did it accumulate so quickly? The outstanding work of Wangensteen, Hibbard and Rea [2] and Singleton and co-workers [3] has established atmospheric air as the major source of gas in distention secondary to acute intestinal obstruction. It would seem that exogenous air must also have been the predominant source in the case cited, for it is almost inconceivable that

Read at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 22, 1947.

From the Departments of Physiology and Surgery, Northwestern University Medical School and Wesley Memorial Hospital, Chicago.

1. Maddock, W. G., and Coventry, M. B.: A Perforated Ulcer of the Ileum Opposite a Meckel's Diverticulum, Surg., Gynec. & Obst. **73**:105, 1941.

2. Hibbard, J. S., and Wangensteen, O. H.: Character of the Gaseous Distention in Mechanical Obstruction of the Small Intestine, Proc. Soc. Exper. Biol. & Med. **31**:1063, 1934. Hibbard, J. S.: Gaseous Distention Associated with Mechanical Obstruction of the Intestine, Arch. Surg. **33**:146 (July) 1936. Wangensteen, O. H., and Rea, C. E.: The Distention Factor in Simple Intestinal Obstruction, Surgery **5**:327, 1939.

3. Singleton, A. O.; Rogers, F., and Houston, F. G.: The Problem of Intestinal Gases Complicating Abdominal Surgery, Ann. Surg. **115**:921, 1942.

fermentation or diffusion could produce so much gas in such a short time. But how could air enter the abdomen so rapidly? The generally accepted explanation would be by air swallowing, which theoretically might have supplied such a volume in a comparatively short period of time. However, repeated swallowing was not observed. Rather it appeared that the child had literally pumped himself up. One of us (A. C. I.) has observed this phenomenon in 2 dogs under light ether

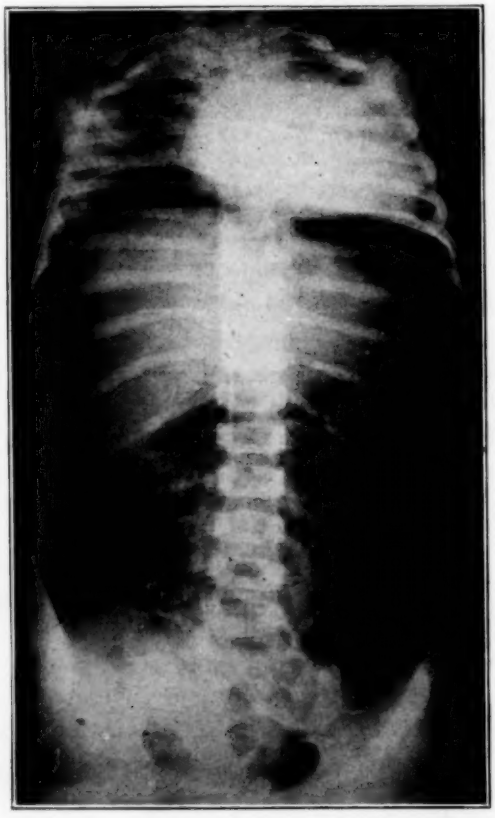

Fig. 1.—Massive pneumoperitoneum in a child following perforation of an ileal ulcer. Note marked distention with extreme encroachment on the thorax.

anesthesia while the gallbladder was being artificially distended. Similarly, Alvarez,[4] referring to several instances in which he had observed acute dilatation of the stomach in experimental animals, stated, "In some instances it was due to a peculiar type of powerful, sighing, respiratory movement which soon pumped the stomach full of air."

4. Alvarez, W. C.: An Introduction to Gastroenterology, New York, Paul B. Hoeber, Inc., 1940, pp. 563-588.

The role of true air swallowing in slowly developing distention was demonstrated by the early work of Kantor and Marks,[5] who showed by combined auscultatory and roentgenographic means that air is actually swallowed in conjunction with the ingestion of food and drink. However, in rapid distention, usually involving larger volumes of gas, frequent, voluntary swallowing is not commonly reported, though one would expect it to be if swallowing were an important factor in the distention mechanism. In the literature only an article by McIver, Benedict and Cline[6] states the number of observed, true swallows. In 3 surgical cases they counted one hundred and fifteen, sixty-seven and forty-four swallowing movements respectively during the induction of ether anesthesia, though the volume of gas recovered from these particular patients was not stated. In another series of patients the average volume of gastric gas "swallowed" between the induction of anesthesia and completion of the operation was 145 cc. Subsequently, Davis and Hansen[7] inserted a Levine tube into the stomachs of 53 patients preoperatively and found that an average of 126 cc. of gas accumulated in the stomach during the operation. No mention was made of observations on swallowing by these patients.

Such a paucity of data by no means constitutes proof of the nonexistence of air swallowing as a factor in acute abdominal distention, nor does it in any way lessen the strong evidence favoring atmospheric air as the chief source of the distending gas. Granted that the air comes down through the esophagus, the question arose whether or not any other mechanism than air swallowing could account for its entry. A review and investigation of other conditions in which atmospheric air can accumulate in the upper part of the gastrointestinal tract seemed warranted. The most pertinent literature concerned acute dilatation of the stomach, air sucking and esophageal speech. These will be commented on and the results of experiments which developed will be reported.

REVIEW OF THE LITERATURE

A. Acute Gastric Dilatation.—Rokitansky,[8] in 1842, first described the postmortem observations in a case in which "the stomach filled the entire abdomen," and this is considered the first report of acute dilatation

5. Kantor, J. L.: A Study of Atmospheric Air in the Upper Digestive Tract, Am. J. M. Sc. **155**:829, 1918. Kantor, J. L., and Marks, J. A.: A Study of Intestinal Flatulence, Ann. Int. Med. **3**:403, 1929.

6. McIver, M. A.; Benedict, E. B., and Cline, J. W., Jr.: Post-Operative Gaseous Distention of the Intestine: Experimental and Clinical Study, Arch. Surg. **13**:588 (Oct.) 1926.

7. Davis, H. H., and Hansen, T. M.: Investigation of the Cause and Prevention of Gas Pains Following Abdominal Operation, Surgery **17**:492, 1945.

8. von Rokitansky, C.: Handbuch der speciellen pathologischen Anatomie, ed. 3, Vienna, Braumüller u. Seidel, 1842, vol. 3, p. 178.

of the stomach. Thirty years later Hilton Fagge [9] recorded the classical clinical description of vomiting, tremendous gaseous and fluid distention of the stomach and collapse. Subsequently epigastric pain, abdominal tenderness, constipation, thirst and oliguria were found to be associated symptoms of variable severity.

Acute dilatation of the stomach is customarily a complication of some preexisting medical or surgical problem. In 90 per cent of the cases vomiting is the presenting symptom,[10] and in surgical patients this may easily be mistaken for the usual postoperative emesis. Characteristically regurgitant, the vomiting amounts to a sort of overflow of a thin, brownish, nonfeculent fluid, often voluminous but affording little relief to the patient.

The most prominent sign of the disease is the tremendous gastric distention. Concerning the volumes involved there are few figures available. Usually only such descriptive terms as "stomach greatly distended, chiefly with gas" [11] or "stomach enormously dilated and reaching down nearly to the pubis" [12] have been found. Laffer [10] reported a case in which the distention was so great that the body could not be placed in a casket. When a trocar was passed into the stomach "a great quantity of gas and a quart of milky fluid escaped" (compound spirit of ether N. F. had been administered). Three cases were found in which the gastric volume could be calculated from reported postmortem measurements of the stomach. In a case reported by Luckett [13] the size of the stomach was 17 by 10 by 7 inches (43.2 by 25.4 by 17.8 cm.), which represents a volume of at least 7,500 cc. More conservative were the postmortem measurements of the stomach in 2 of Moore's [14] cases, from which the volumes were calculated to be 3,000 cc. and 2,600 cc. respectively. Thomas and Harper [15] recently reported a case in which they aspirated 2,000 cc. of gas.

The rapidity with which enormous acute gastric dilatation develops has been frequently commented on, but seldom with the desired accuracy. However, 11 cases have been collected in which there were notations

9. Fagge, C. H.: Acute Dilatation of the Stomach, Guy's Hosp. Rep. **18**:1, 1873.

10. Laffer, W. B.: Acute Dilatation of the Stomach and Arterio-Mesenteric Ileus, Ann. Surg. **47**:390, 1908.

11. Thomson, H. C.: Acute Dilatation of the Stomach, New York, William Wood & Company, 1902.

12. Broadbent, W., cited by Thomson.[11]

13. Luckett, W. H.: Visible Acute Dilatation of the Stomach During Laparotomy, J. A. M. A. **64**:2055 (June 19) 1915.

14. Moore, J. W.: Gastromesenteric Ileus, New York, M. J. **105**:544, 1917.

15. Thomas, C. A., and Harper, F. R.: Acute Dilatation of the Stomach Following Left-Sided Phrenic Paralysis and Thoracoplasty, J. Thoracic Surg. **5**:507, 1935.

of the distention time or sufficient data from which it could be roughly estimated. These are shown in table 1; and it is apparent that marked distention occurred within fifteen minutes or less in 8 of the 11 cases.

The alleged factors causing acute gastric dilatation are both numerous and diverse, almost every common medical and surgical condition having been implicated. Borchgrevink,[16] reporting a series of 144 unselected cases, related 44 different predisposing causes. These, with a few additions, are shown in table 2. Sex, race, occupation or environment have not been found to be etiologically significant and no age is exempt, for Belilios[17] saw acute gastric dilatation in a 9 month old baby, while Moore[14] recorded the case of an 86 year old man.

To account for acute dilatation of the stomach many theoretic hypotheses have been proposed, as indicated by the following synonyms

TABLE 1.—*The Rate of Distention in Acute Dilatation of the Stomach*

Author	Distention Time	Degree of Distention
Doolin[20]	"Few minutes"	"Alarming size"
Laffer[19]	Less than one hour	"Greatly distended"
Lee, B. J.: Ann. Surg. **63**: 418, 1916	5 to 15 minutes	"Enormously dilated"
Luckett[13]	15 minutes	"Tremendous distention"
Mallory, T. B.: New England J. Med. **219**: 166, 1938	Less than two hours	"Tremendous distention"
Mayoral, A., Jr.: J. A. M. A. **64**: 146, 1915	5 to 10 minutes	Distended to within three fingerbreadths of the symphysis pubis
McIver[35]	5 minutes	Dilatation
Moorhead, E. L.: J. A. M. A. **52**: 1806, 1909	5 minutes	Distention to midpoint between the umbilicus and pubis
Novak, E.: J. A. M. A. **77**: 81, 1921	"Less than 30 seconds"	"Enormous size"
Richardson, W. G.: Brit. M. J. **2**: 1202, 1913	5 to 10 minutes	Distended
Thomas and Harper[15]	"Within 30 minutes"	"Enormous distention"

commonly employed: acute gastroduodenal atony, acute postoperative gastric paralysis, gastroenteroplegia, gastrorrhea and acute gastromesenteric ileus.

The atonic theory, first mentioned by Brinton in 1859,[18] holds that acute dilatation of the stomach is the result of a reflex disturbance of the extrinsic gastric innervation. This allegedly produces gastric atony, as a result of which gases and fluids ordinarily formed in the stomach and intestines are permitted to accumulate rather than being absorbed

16. Borchgrevink, O. J.: Acute Dilatation of the Stomach and Its Treatment, Surg., Gynec. & Obst. **16**:662, 1913.

17. Belilios, D. A.: Acute Dilatation of the Stomach Without Apparent Cause, Brit. M. J. **1**:74, 1903.

18. Brinton, W.: Lectures on Disease of the Stomach, ed. 1, London, John Churchill & Sons, 1859, pp. 291-300.

or expelled. The significance of atony in permitting the accumulation of large volumes of gastric gas was demonstrated by Kelling [19] and Braun and Seidel,[20] who through gastric fistulas artificially distended the stomachs of conscious dogs until eructation occurred. In the same animals under anesthesia or after vagotomy they found that two to three times greater distention could be maintained without eructation. However, such evidence supplies only a negative factor in explanation of the atonic theory, for it stresses loss of tone without offering any proved positive mechanism to account for the distending gas.

TABLE 2.—*Reported Causal Factors in Acute Dilatation of the Stomach*

Abdominal and Pelvic Operations		
Gastrointestinal	**Biliary Tract**	**Genital Tract**
Appendectomy	Cholecystectomy	Cesarean section
Bowel anastomosis	Cholecystostomy	Anterior colporrhaphy
Gastroduodenostomy	Drainage of hepatic abscess	Hysterectomy
Gastrojejunostomy		Oophorectomy
Gastrostomy		Perineorrhaphy
Herniorrhaphy		Salpingectomy
Pyloric resection		Uterine fixation
Extra-Abdominal Operations		
Urinary Tract	**Extremities**	**Thorax**
Nephrectomy	Amputations	Phrenicotomy *
Nephropexy	Hip joint resections	Thoracoplasty *
Urethrostomy	Osteotomy	Vagotomy *
Acute and Chronic Diseases		
Cholecystitis	Maxillary sinusitis	Scarlet fever
Diabetes	Pneumonia	Sciatica
Endocarditis	"Rheumatism"	Tuberculosis
	Typhoid	
Deformities		
Lumbodorsal scoliosis	Spinal tuberculosis	
Spondylolisthesis		
Miscellaneous		
Anesthesia (general, spinal, local)	Application of body cast	
Childbirth	Abdominal trauma	
Fractures	Ureteral catheterization	
Paraplegia	Dietary indiscretion	

* Added from other sources.

Often cited in support of the atonic theory are the reports of Hartwell,[21] Carion and Hallion [22] and Smith,[23] who claimed to have observed or produced acute dilatation of the stomach by cervical, transthoracic

19. Kelling, G.: Ueber den Mechanismus der acuten Magendilatation, Arch. f. klin. Chir. **64**:393, 1901.

20. Braun, W., and Seidel, H.: Klinisch-experimentelle Untersuchungen zur Frage der akuten Magenerweiterung, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **17**: 533, 1907.

21. Hartwell, J. A., in discussion on Moschcowitz, A. V.: Gastromesenteric Ileus Following a Cholecystectomy, Ann. Surg. **55**:614, 1912.

22. Carion and Hallion: Dilatation de l'estomac par section des nervos vagues, Bull. méd., Paris **9**:809, 1895.

23. Smith, H. B.: Postoperative Acute Dilatation of the Stomach, Boston M. & S. J. **161**:529, 1909.

or subdiaphragmatic vagotomy. None of these authors presented sufficient data to permit repetition of their work or proper evaluation of their results. Furthermore, vagotomy has been produced thousands of times in dogs and several hundred times in human beings with only an occasional case of true acute, gaseous, gastric dilatation occurring as a complication,[24] though immotility and some degree of gastric atony may be a frequent postoperative finding.

The theory of duodenal obstruction was proposed by von Rokitansky [25] in 1861. It stated that acute dilatation of the stomach is nothing more than a high intestinal obstruction occurring in the third portion of the duodenum, the obstructing element being the mesentery and superior mesenteric vessels overlying the duodenum as it crosses the spine. Kundrat [26] first reported 3 cases which illustrated this type of mechanical obstruction, and subsequently Albrecht,[27] Muller,[28] Schnitzler [29] and others, having observed this condition in their own cases, joined in endorsing the theory. Since duodenal obstruction was actually found in only 20 to 25 per cent of cases in which autopsy was performed,[30] controversy arose as to whether this was a primary phenomenon or secondary to the gastric distention, which pushed the intestines into the pelvis, thereby tensing the mesentery and the vessels crossing the duodenum. L. R. and C. A. Dragstedt [31] by obstructing the third portion of the duodenum in 5 dogs showed that though severe toxic symptoms developed within seventy-two hours the stomachs remained small. They concluded that primary duodenal obstruction did not cause acute dilatation of the stomach, but proposed that if duodenal obstruction occurred secondary to gastric distention it could account for the severe toxic symptoms and collapse frequently seen.

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24. Jones, C. M., in discussion on Grimson, K. S.; Ruffin, J. M., and Hollander, F.: Discussion on Symposium on Peptic Ulcer with Particular Reference to Vagotomy, Gastroenterology **7**:615, 1946.

25. von Rokitansky, C.: Lehrbuch der pathologischen Anatomie, ed. 3, Vienna, W. Braumüller, 1861, vol. 3.

26. Kundrat: Ueber eine seltene Form der inneren Incarceration, Wien. med. Wchnschr. **41**:352, 1891.

27. Albrecht, P. A.: Ueber arterio-mesenterialen Darmverschluss an der Duodeno-Jejunalgrenze und Seine ursachliche Beziehung zur Magenerweiterung, Virchows Arch. f. path. Anat. **156**:285, 1899.

28. Muller, P.: Ueber akute postoperative Magendilatation, hervorgerufen durch arteriomesenteriale Duodenal-Kompression, Deutsche Ztschr. f. Chir. **56**: 486, 1900.

29. Schnitzler, J.: Ueber mesenteriale Darmincarceration, Wien. klin. Rundschau **9**:579, 1895.

30. Doolin, W.: Acute Dilatation of the Stomach, Brit. J. Surg. **6**:125, 1918. Laffer.[10]

31. Dragstedt, L. R., and Dragstedt, C. A.: Acute Dilatation of the Stomach, J. A. M. A. **79**:612 (Aug. 19) 1922.

In 1912, Woodyatt and Graham [32] advanced the theory that acute dilatation of the stomach is due to gastric secretion of gas, the result of interference with oxidative processes in the wall of the stomach as a sequela of local impairment of blood supply, general asphyxia or poisoning. The theory was based on the early work of Schierbeck,[33] who reported high tensions of carbon dioxide in the stomach during the height of digestion. However, this later work has since given way to the conclusive observations of McIver, Redfield and Benedict [34] that the tensions of gases of the alimentary tract tend to approach those of the blood, obeying the laws of physical diffusion.

It seems apparent from the foregoing review that the mechanism of acute dilatation of the stomach still remains obscure and confused. Most of the contributions to the subject have been efforts to explain the cause of the disease, while careful observations that might have given a clue to the source of the gas and its mode of transport to the stomach have been minimal. In few of the cases reviewed was air swallowing even suggested as the means of accumulation of gas. Rather, one keen observer, Luckett,[13] reporting a case in which acute distention occurred during surgical treatment, stated: "I could distinctly feel and hear large gulps of air entering the stomach, and hear a noise in the throat; yet the patient was not swallowing; that is, the thyroid cartilage was apparently still and there was no visible motion in the throat." Similarly, McIver [35] recorded 3 cases of acute dilatation of the stomach during surgical treatment in which he stated that the occurrence of swallowing was not noted either by himself or by the anesthetist. Since many reported cases of acute dilatation of the stomach have occurred during administration of a general anesthetic when the swallowing reflex might reasonably be expected to have been largely abolished, further doubt is cast on the role of ordinary swallowing as an important factor in the mechanism of this disease.

Though not ordinarily considered of significance in the mechanism of acute gastric dilatation, the possible importance of abnormal respiration has been suggested. Mention has been made of Alvarez's [4] comment of having observed peculiar, powerful respiratory movements pump the stomach full of air, and Klemptner [36] in reviewing the caus-

32. Woodyatt, R. T., and Graham, E. A.: Alimentary Respiration, Ohio State M. J. **8**:407, 1912.

33. Schierbeck, N. P.: Skandinav. Arch. f. Physiol. **3**:437, 1892.

34. McIver, M. A.; Redfield, A. C., and Benedict, E. B.: Gaseous Exchange Between the Blood and the Lumen of the Stomach and Intestines, Am. J. Physiol. **76**:92, 1926.

35. McIver, M. A.: Acute Dilatation of the Stomach Occurring Under General Anesthesia, Ann. Surg. **85**:704, 1927.

36. Klemptner, D.: The Cause of Acute Dilatation of the Stomach, Illinois M. J. **68**:159, 1935.

ation of this disease said: "A common factor in all cases of acute dilatation of the stomach associated with surgery is a disturbed respiratory mechanism." Specific references to the character of the respiration in acute gastric dilatation are seldom made, though in Thomson's [11] series of 44 cases 9 presented respiratory abnormalities as follows: pneumonia and/or pleurisy 4, pulmonary edema 2, empyema 1, marked dyspnea 1 and hiccups 1.

B. Air Sucking.—Weissgerber [37] credited Kehrer in 1877 with first suggesting that air could be "sucked" into the stomach. Though few details are reported, Kehrer is said to have inserted a small rubber tube through the esophagus into the stomach of newborn infants and with an attached mercury manometer recorded subatmospheric intragastric pressures during the inspiratory phase of respiration. Actual figures were not recorded, but the author concluded that such "respiratory sucking" accounted for the free gas in the stomach and intestines of the newborn. Studying 7 newborn infants, Paine and Nessa [38] roentgenographically demonstrated gas in some part of the upper gastrointestinal tract within fifteen minutes after birth. Dillon,[39] in an article on "The Respiratory Function of the Digestive Tract as the Basis of a Roentgenographic Life Test," stated that carefully verified roentgenologic investigations "prove" that air may penetrate into the stomach without any gulping movement, such "stomach respiration" accounting for the air bubble ordinarily seen in the cardiac end of the stomach.

Wyllie [40] in 1895 wrote an exceedingly interesting article carefully describing the mechanism of "air sucking," whereby air could be introduced into the upper part of the alimentary tract without swallowing. After studying 3 students who performed this act voluntarily he related the procedure briefly as follows: Elevate the chin and extend the neck to pull the larynx forward; then make an inspiratory effort against a closed glottis. By direct laryngoscopic examination of the upper end of the esophagus during the act he observed that this position produced a small opening in the normally closed sphincter at the pharyngeoesophageal junction, referred to as the superior esophageal sphincter [40a]

37. Weissgerber, P.: Ueber den Mechanismus der Ructus und Bemerkungen über den Lufteintritt in den Magen Neugeborener, Berl. klin. Wchnschr. **15**:521, 1878.

38. Paine, J. R., and Nessa, C. B.: Observations on the Distribution and Transport of Gas in the Gastrointestinal Tract of Infants and Young Children, Surgery **11**:281, 1942.

39. Dillon, J. G.: The Respiratory Function of the Digestive Tract as the Basis of Roentgenographic Life Test, Am. J. Roentgenol. **48**:613, 1942.

40. Wyllie, J.: On Gastric Flatulence, Edinburgh Hosp. Rep. **3**:21, 1895.

40a. Killian, G.: Ueber den Mund der Speiseröhre, Ztschr. f. Ohrenh. **55**:1, 1908.

(this structure will be described later). With each inspiratory effort against a closed glottis air readily entered the esophagus and was belched during expiration or passed on into the stomach if eructation was suppressed. Such air sucking is known to be a fairly common accomplishment of adolescent boys, who learn the procedure to become the most proficient "belcher" in their group. Such persons will be referred to in this article as air suckers.

Intake of air during this act is apparently due to the negative pressure developed during inspiration, for the esophagus is subject to the changes in pressure that develop in the intrapleural space.[41] Though negative intrapleural and thus intraesophageal pressures as low as minus 40 mm. of mercury have been shown to develop during inspiration against an obstruction,[42] McIver [35] demonstrated in anesthetized cats that the negative intraesophageal pressure developed during unobstructed inspiration could "aspirate" air through a rigid tube passed into the esophagus. When a one way valve prevented its escape on expiration the air accumulated in the stomach, having been propelled from the esophagus by peristalsis or an esophageal-gastric pressure gradient. To account for a possible valvelike action in man McIver postulated that the soft palate or the tongue might drop back, obstructing the escape of air from the esophagus on expiration. However, it seems apparent that such an obstruction would also interefere with pulmonary expiration, resulting in elevation of the intrapleural and consequently the intraesophageal pressure, which would tend to force the air out of the esophagus. As will be brought out later, the possibility of a valvelike action of the superior esophageal sphincter seems a more likely explanation, for it would obstruct the escape of intraesophageal air without interfering with pulmonary expiration.

C. Esophageal Speech.—Continued search for knowledge of any condition in which air enters the upper alimentary tract without swallowing led to a consideration of the subject of esophageal speech. After a laryngectomy many patients have been taught to "aspirate" air into the esophagus during inspiration, then eructate it back to produce vibrations of the superior esophageal sphincter, such vibrations being then converted into speech by the oral structures.

Morrison [43] stated that proficiency in esophageal speech depends on the character of the musculature of the pharyngoesophageal junc-

41. Heynsius, A.: Ueber die Grosse des negative Drucks im Thorax beim ruhigem Athmen, Arch. f. d. ges. Physiol. **29**:265, 1882.

42. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 4, Baltimore, Williams & Wilkins Company, 1945, pp. 297-298.

43. Morrison, W. W.: The Production of Voice and Speech Following Total Laryngectomy: Exercise and Practice for Production of ‚Pseudovoice, Arch. Otolaryng. **14**:413 (Oct.) 1931.

tion (cricopharyngeus muscle) and the ability of the subject voluntarily to relax the superior esophageal sphincter, so that air can be taken in without swallowing. Stetson [44] has further shown that the part played by the chest in esophageal speech is greater than normal, for the intake of air is dependent on the negative intraesophageal pressure developed during inspiration.

Patients must learn to retain the aspirated air in an esophageal reservoir; otherwise it will be propelled on into the stomach by peristalsis. This was demonstrated experimentally by Quinche,[45] who introduced air into the esophagus in dogs and found that within four to five seconds it had been propelled into the stomach. That this unavoidably occurs in patients being taught esophageal speech was shown fluoroscopically in more than 50 per cent of 100 patients studied by Stern.[46] Similarly, Morrison [47] stated that in many patients some of the aspirated air "slips into the stomach where it increases the size of the gastric air bubble," while others less satisfactorily used the stomach rather than the esophagus as their air reservoir. It is interesting to note at this point that many ventriloquists are said to utilize esophageal speech for their manikin,[39] and the German word for ventriloquism, "Bauchredner," is a combination of two words meaning belly speech.

The similarity between the mechanisms of air intake in air sucking and in esophageal speech is apparent. The procedure for the former is described as elevation of the chin and extension of the neck to pull the larynx forward, while making an inspiratory effort against a closed glottis. On the other hand laryngectomized patients being taught esophageal speech, while first learning, are instructed to elevate the hyoid bone and "close the tracheal opening with their finger, then attempt to insufflate air into the esophagus during the act of chest expansion."[48] In both instances the act is dependent on relaxation of the superior esophageal sphincter while a negative intraesophageal pressure is developed by inspiration. It is conceivable that this mechanism, or some modification of it, may occur in acute dilatation of the stomach and other commoner types of acute abdominal distention.

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44. Stetson, R. H.: Esophageal Speech for Any Laryngectomized Patient, Arch. Otolaryng. **26**:132 (Aug.) 1937.

45. Quinche, H.: Ueber Luftschlucken und Schluckgerausche, Arch. f. exper. Path. u. Pharmakol. **22**:385, 1887.

46. Stern: Der Mechanismus der Sprech-und Stimmbildung bei Laryngektomierten, und die derartigen Fallen angewandte Uebungstherapie, in Denker, A., and Kahler, O.: Handbuch der Hals-Nasen-Ohrenheilkunde, mit Einschluss der Grenzgebiete, Berlin, Julius Springer, 1926, vol. 5, p. 494.

47. Morrison, W.: Physical Rehabilitation of the Laryngectomized Patient, Arch. Otolaryng. **34**:1101 (Dec.) 1941.

48. Gatewood, E. T.: The Mechanism of Esophageal Voice Following Laryngectomy, Virginia M. Monthly **71**:9, 1944.

EXPERIMENTAL METHODS AND RESULTS

A. Experiments on Animals.—The most direct approach to the study of the mechanism involved in acute gastric distention seemed to be to produce this condition in animals, and then to observe and record the factors involved in the process. Taking suggestions from several reports of the intentional and unintentional development of acute distention of the stomach found in the literature, we made attempts to reproduce such results in dogs. The methods employed and the results obtained are briefly recorded in table 3. Since none of the methods employed consistently produced acute distention, only the results of two associated experimental studies will be discussed.

As was previously mentioned, McIver [38] produced acute gastric distention in anesthetized cats by inserting a glass tube with a one way valve into the upper part of the esophagus. Since the tube merely overcame or eliminated the action of the superior esophageal sphincter, it became apparent to us that this structure must be the normal obstructing mechanism to the ingress of air into the esophagus without swallowing. Anatomically, in the dog, this sphincter was found to be composed of a well formed mucosal fold with a circular lip directed caudad, as shown in figure 2. This structure was found at the pharyngoesophageal junction at the same level as the transverse fibers of the inferior pharyngeal constrictor muscle, and together the mucosal fold and the constrictor muscle fibers form the superior esophageal sphincter, first described by Killian [40a] in 1908. Like other sphincters of the alimentary tract it should favor the ingress of matter while preventing the escape cephalad.

In view of these facts it was considered pertinent to determine whether the tone of the superior esophageal sphincter could be decreased sufficiently to allow the ingress of air into the esophagus coincident with the negative intraesophageal pressure developed during inspiration. First, a reflex was sought that might relax the sphincter tone or cause the structure to act as a one way valve. Because of the high incidence of acute distention following abdominal surgical treatment, intra-abdominal stimuli were considered most likely to produce such an effect. Secondly, denervation of the sphincter was performed to determine whether this would reduce its tone and permit entry of air.

1. Effect of Intra-Abdominal Stimuli on Tone of Superior Esophageal Sphincter: In 8 dogs anesthetized with ether a small recording balloon was inserted into the superior esophageal sphincter and attached by a rubber tube to a water manometer which recorded on a revolving kymograph drum. Simultaneously tracings of respiratory and swallowing movements were made. With this arrangement stimulation of the celiac and mesenteric plexuses, splanchnic nerves, sympathetic trunks and celiac artery was carried out with faradic current. In addition,

TABLE 3.—*Summary of Attempts to Produce Acute Gastric Distention in Dogs*

Procedure	No. of Trials	Indication	Results
1. Vagotomy			
a. Transthoracic	5	Report of Carlon and Hallion [22]	Failure
(1) Plus phrenicotomy	1	Report of Thomas and Harper [15]	Failure
b. Cervical	2	Report of Hartwell [31]	Failure
c. Subdiaphragmatic	2	Report of Smith [23]	Failure
(1) Plus duodenal obstruction	1	Report of Smith [23]	100 cc. of gas and fluid in 24 hours
(2) Plus intravenous and oral administration of antimony potassium tartrate	2	Report of Braun and Seidel [20]	No vomiting; no distention
(3) Plus intra-abdominal stimuli	1	High incidence of acute distention associated with laparotomy	Failure
2. Gastric vascular ligation	1	Report of Woodyatt and Graham [32]	Failure
3. Duodenal obstruction (3d portion)	1	Report of Kundrat [26]	Small volume of fluid and gas in 24 hours
4. Gastric torsion			
a. 90° clockwise	1	Report of Blackburn, P. S., and McFarlane, D.: J. Comp. Path. & Therap. **54** : 189, 1944	Failure
b. 270° counterclockwise	1		Failure
5. Intestinal irritation with croton oil			
a. In cecum	1	Report of Hedbloom, C. A., and	Failure
b. In ileum	1	Cannon, W. B.: Am. J. M. Sc. **138** : 504, 1909	Failure
6. Irritation of peritoneum with HCl	1	Acute distention associated with chemical peritonitis	Failure
7. Retroperitoneal injection of blood	2	Report of Phillipe, C.: Presse méd. **1** : 60, 1909	Failure
8. Cervical vagal stimulation (Faradic current)			
a. Bilateral intact and transected central and distal ends	3	Report of Meltzer, S. J., and Auer, J.: Proc. Soc. Exper. Biol. & Med. **3** : 74, 1905-1906	Contraction of esophagus; no distention
b. Same as (a) with superior esophageal sphincter intubated	3	Report of Meltzer and Auer and of McIver [35]	Contraction of esophagus; no distention
9. Ureteral distention	2	Report of Magnusson, W.: Acta radiol. **12** : 552, 1931	Failure
10. Intra-abdominal stimuli (effect on secondary peristalsis)			
a. Distention of gallbladder	2	To determine whether these stimuli would cause secondary peristalsis to transport air	Failure
b. Duodenal distention	2		
c. Manual manipulation of organs of upper part of abdomen	2		
11. Manually "ball-valving" the intubated esophagus			
a. Alone	2	Report of McIver [35]	Distention in anesthetized dogs only
b. After subdiaphragmatic vagotomy	2	Report of McIver [35] plus effect of atony	Appreciable distention in anesthetized dogs only
c. After transthoracic vagotomy	1	Report of McIver [35] plus effect of atony	Appreciable distention in anesthetized dogs only
12. Intra-abdominal stimuli (effect on tone of upper esophageal sphincter)			
a. Distention of gallbladder	2	To determine whether any intra-abdominal stimuli would reflexly affect tone of superior esophageal sphincter	Failure
b. Duodenal distention	2		Failure
c. Trauma of abdominal viscera	2		Failure
d. Chemical irritation of peritoneum with 95% alcohol	1	.....	Failure
e. Stimulation of superior mesenteric and/or celiac ganglion	4	.....	Failure
f. Subdiaphragmatic vagal stimulation	17	.....	Fluctuations in sphincter tone in 7 dogs; acute distention in 3 dogs
13. Denervation of superior esophageal sphincter			
a. By procaine infiltration	1	To determine whether paralysis of the superior esophageal sphincter would permit entry of air into the esophagus during respiration	Failure
b. By multiple nerve section	1		
c. By transection of the pharyngeal branch of the vagus	1		
14. Distention of the vagotomized stomach	3	To determine whether the picture of acute dilatation of the stomach could be produced	Failure

severe trauma to the bowel by tamponade and traction, distention of gallbladder and duodenum with balloons and chemical irritation of the peritoneum with alcohol were tried. Eleven such procedures in 8 dogs did not result in any appreciable change in the tone of the superior esophageal sphincter. In 7 of another series of 17 lightly anesthetized dogs subdiaphragmatic vagal stimulation with moderately intense faradic current produced a short period of apnea followed by hyperpnea, vigorous clonic contractions of the diaphragm and pronounced fluctu-

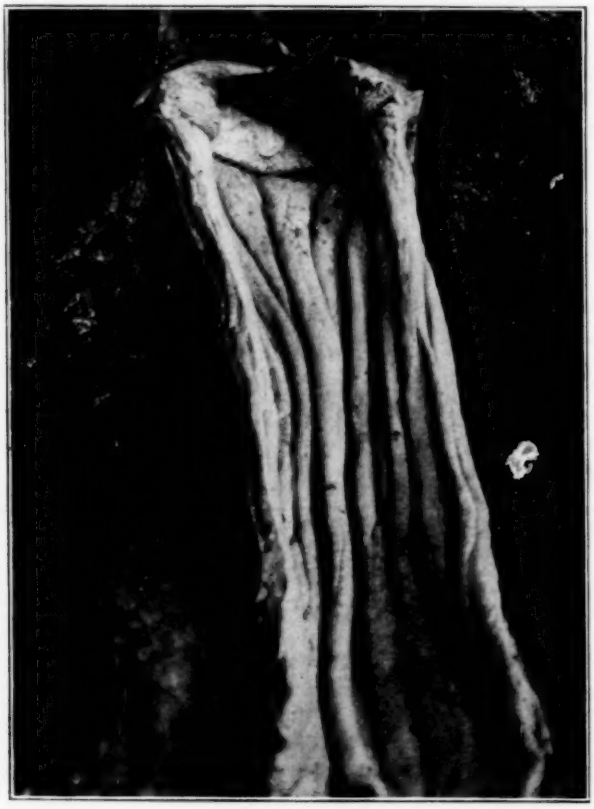

Fig. 2.—Superior esophageal sphincter in the dog. Note that the lip is directed caudad.

ations in tone of the superior esophageal sphincter. A typical tracing is shown in figure 3. In 3 instances definite acute gastric distention occurred coincident with this phenomenon, the stomach protruding through the abdominal wound and necessitating release of 250 to 400 cc. of gas with a syringe and needle before the stomach could be replaced in the abdominal cavity. Though the source of gas and the actual mechanism involved in its transport could not be definitely ascertained in these instances, true swallowing was not seen to occur. The rate of accumulation of gas in these dogs, thirty to sixty seconds, favors an exogenous

source, and the concurrent powerful respiratory excursions seemed to be an important part of the process.

That the upper esophageal sphincter acted as a one way valve is unlikely, for kymograms of this phenomenon made on a rapidly revolving drum showed increased sphincter tone during inspiration and relaxation during expiration. It was considered that the recorded activity of the sphincter might merely be secondary to vigorous respiratory excursions, but in 2 instances the number of fluctuations in sphincter tone did not correspond with the number of deep respirations. Furthermore, tachypnea produced by intravenous injection of 1 cc. of air per kilogram of body weight and hyperpnea induced by the intravenous injection of 15 cc. of dilute hydrochloric acid failed to produce comparable fluctuations in the tone of the esophageal sphincter.

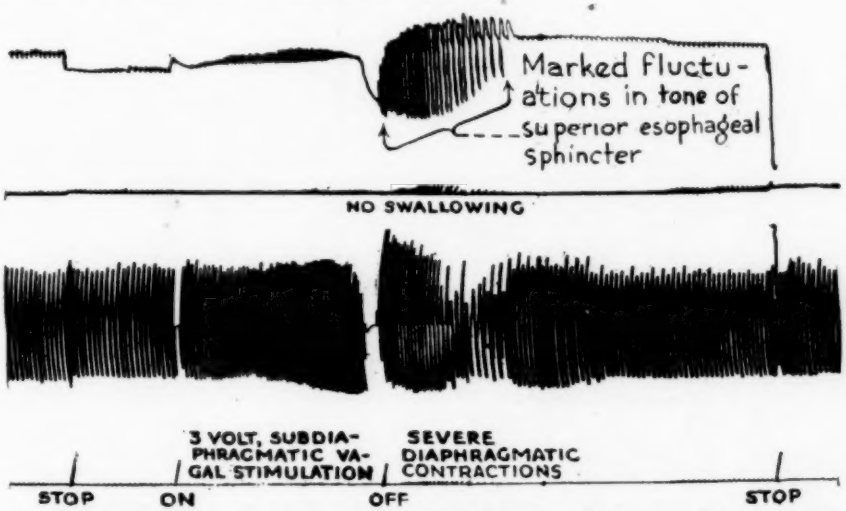

Fig. 3.—Water manometer tracing showing the effect of subdiaphragmatic vagal stimulation on activity of superior esophageal sphincter. Top tracing, activity of esophageal sphincter. Second tracing, record of swallowing. (Small elevations do not represent swallows but are due to movement of recording equipment as a result of violent respiratory excursion.) Third tracing, respiration. Bottom tracing, stimulus.

2. Denervation of the Superior Esophageal Sphincter: Since the tone of the superior esophageal sphincter normally prevents entrance of air into the esophagus, this structure was denervated in 2 dogs to determine the effect. In one a midline cervical incision was made with the dog under ether anesthesia, and the larynx, trachea and upper part of the esophagus were exposed. All the structures in the region of the upper part of the esophagus were infiltrated with 2 per cent procaine and the wound was closed. On immediate recovery from the general anesthetic and on periodic observations for the next seventy-two hours no signs of abdominal distention developed. A second dog was subjected to bilateral

surgical transection of all visible nerves in the vicinity of the hypopharynx and upper end of the esophagus. This dog was unable to swallow food or water on recovery from the operation, and during the observed period of six days no distention developed.

Experimental work on esophageal innervation now being carried out by Hwang, Grossman, and Ivy at the University of Illinois has revealed that a small nerve, apparently arising just above the ganglion nodosum of the vagus, supplies the main motor innervation to the cervical part of the esophagus in the dog. Its control over the superior esophageal sphincter has not been established, but experiments are contemplated to determine the effect of bilateral transection of this nerve.

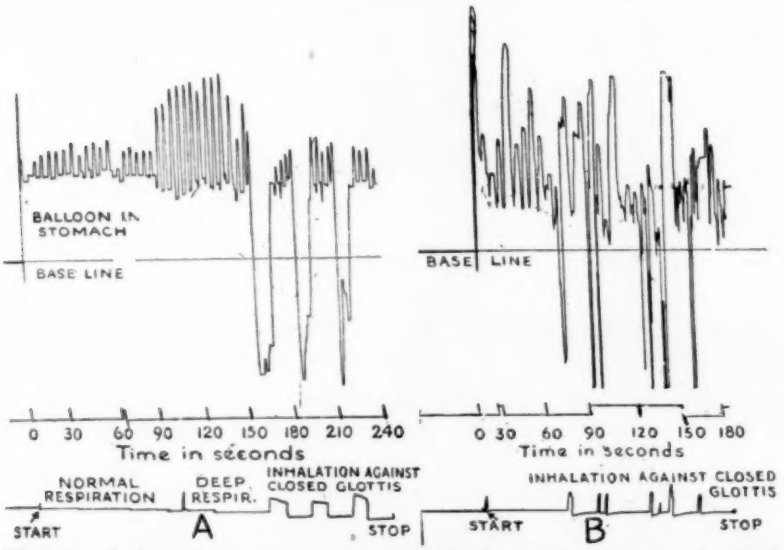

Fig. 4.—*A*, bromoform manometer tracing of negative intragastric pressure developed during inspiration against a closed glottis. *B*, bromoform manometer tracing (tube in lower part of esophagus) of negative intraesophageal pressure developed during inspiration against a closed glottis.

B. Experiments on Human Beings.—The inability to produce acute distention consistently in dogs nullified any attempts to determine the mechanism by this means. On the basis of recorded descriptions of air sucking it seemed relevant to study the factors involved in this act to determine their applicability to the mechanism of acute distention.

1. Intraesophageal and Intragastric Pressures Developed During Inspiration Against a Closed Glottis: First, the intragastric pressure developed during inspiration against a closed glottis was determined. Each of 7 subjects swallowed a small Levine tube until the attached recording balloon lodged in the cardiac end of the stomach. The external end of the tube was then attached to a bromoform manometer and the balloon inflated with 30 to 40 cc. of air. After a short normal recording

on a slowly revolving kymograph the seated subject was first directed to make several inspiratory efforts against a closed glottis. Then in 3 subjects the balloon was deflated and withdrawn to the level of the lower part of the esophagus, where it was fixed and reinflated with 5 to 10 cc. of air. After a short control period the subjects again made inspiratory efforts against a closed glottis while additional tracings were made. Typical tracings are shown in figure 4, while the summarized results converted to water pressure are recorded in table 4. It is apparent from the results that inspiration against a closed glottis converted a normally positive intragastric pressure of + 2 to + 16 cm. of water [50] to an average negative pressure of — 29.6 cm. of water. Similarly, the same act markedly increased the normally negative intraesophageal pressure from — 6 cm. to — 31.1 cm. of water.

2. Volumes of "Aspirated" Air: (*a*) During air sucking. The volume of air that could be "aspirated" per sucking effort by 5 subjects

TABLE 4.—*Negative Pressures Created During Inspiration Against a Closed Glottis*

Intraesophageal			Intragastric		
Subject	Number of Efforts at Inspiration	Average Pressure, Cm./H_2O	Subject	Number of Efforts at Inspiration	Average Pressure, Cm./H_2O
1.....	4	—25.9	1.....	4	—20.5
2.....	7	—33.9	2.....	5	—32.9
3.....	5	—33.5	3.....	3	—34.2
			4.....	2	—34.8
			5.....	5	—23.6
			6.....	3	—31.8
			7.....	3	—29.2
Average.....		—31.1	Average.....		—29.6

capable of sucking air was determined. Each subject swallowed a small Levine tube so that the end lodged in the cardiac end of the stomach. The external end of the tube was then connected to an empty, slightly overbalanced, recording spirometer, as shown in figure 5. Swallows were recorded simultaneously by a rubber diaphragm fitted over the thyroid cartilage and connected to a recording tambour. The seated subject was then directed to suck in air and suppress swallowing and belching. As air was taken in through the esophagus it accumulated in the stomach and passed up into the spirometer bell through the Levine tube. The volume of air "aspirated" was recorded on a revolving kymograph drum. A typical tracing is shown in figure 6, while the results are recorded in table 5. It was found that an average of 112.3 cc. of air was aspirated into the stomach per sucking effort. No attempt was made to determine the maximum volume of air that could be aspirated per unit time.

49. Footnote deleted.

50. Moritz: Studien über die motorische Thätigkeit des Magens, Ztschr. f. Biol. **32**:313, 1895. Wilson, M. J., and Irving, L.: Pressure in the Stomach, Canad. M. A. J. **25**:685, 1931.

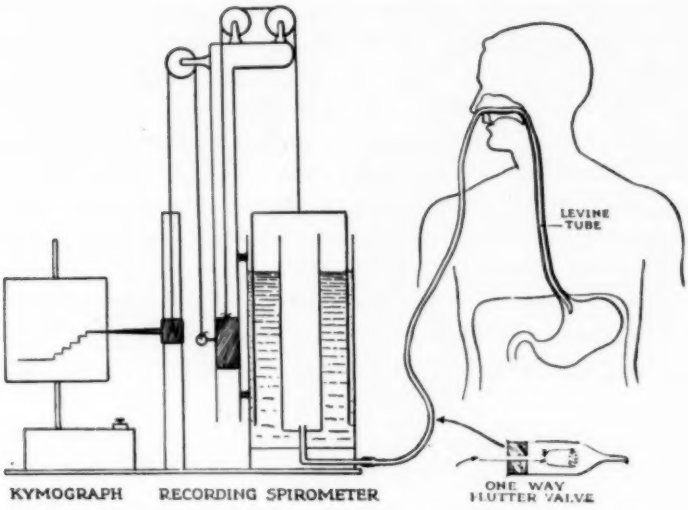

Fig. 5.—Apparatus utilized in recording volumes of gastric gas.

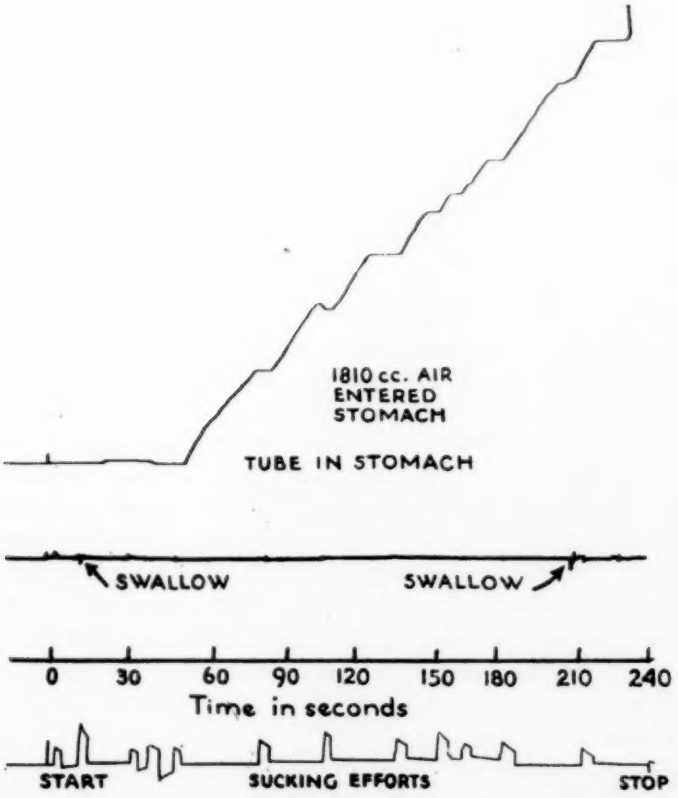

Fig. 6.—Recording spirometer tracing of air "aspirated" into the stomach by air sucking.

(*b*) During inspiration against a closed glottis. Generally, "non-air-suckers" are unable to aspirate air, probably because they have not learned to relax voluntarily the superior esophageal sphincter. However, 3 such subjects were studied according to the previous procedure except that this time the spirometer was filled with air and instead of being directed to suck air they were told to make inspiratory efforts against a closed glottis. The negative pressure thus developed in the stomach withdrew air through the Levine tube from the spirometer bell. A one way flutter valve inserted in the recording apparatus, as shown in figure 5, prevented the air taken into the stomach from returning to the spirometer, and as the aspirated air accumulated in the stomach the subject eructated. Volumes of air aspirated in this manner are given in table 6; they averaged 60.2 cc. per effort.

TABLE 5.—*Volume of Air Aspirated into Stomach by Air Sucking*

Subject	Number of Sucking Efforts	Volume, Cc.	Cc. per Effort
1	25	1,248.2	49.9
2	7	1,000.0	142.9
3	10	1,748.7	174.9
4	16	2,060.3	128.8
5	12	1,803.1	150.3
Average	14	1,572.1	112.3

TABLE 6.—*Volume of Air Aspirated into Stomach by Inspiration Against a Closed Glottis*

Subject	Number of Efforts at Inspiration	Volume, Cc.	Cc. per Effort
1	3	484.4	161.5
2	12	504.5	42.0
3	8	401.2	50.1
Average	7.7	463.4	60.2

(*c*) During respiration. In 5 normal subjects the volume of air which could be "aspirated" into the intubated esophagus during respiration was determined. This was done by having the subject swallow a Levine tube until the tip lodged in the lower third of the esophagus. The external end of the tube was connected to a recording spirometer which contained air in the bell. A one way flutter valve inserted in the tube between the spirometer and the subject, as shown in figure 5, permitted air to move from the spirometer to the esophagus but not in the reverse direction. The subject was then directed to breathe (1) normally, (2) moderately deeply and (3) deeply for five minutes each, while the volume of air aspirated from the spirometer bell into the esophagus was recorded. A typical tracing is shown in figure 7, and the results are recorded in table 7.

It is apparent that the negative intraesophageal pressures created during the inspiratory phase of respiration were sufficient to aspirate air into the esophagus when the superior esophageal sphincter was intubated. Minute volumes being calculated, the average results amounted to 39.5, 43.7 and 91.9 cc. of air per minute during normal, moderate and deep respiration respectively. Thus, in one minute of very deep

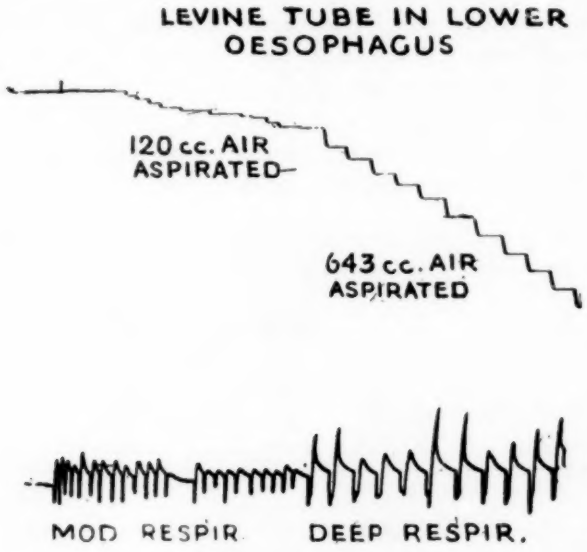

Fig. 7.—Record of air "aspirated" into the esophagus during five minutes of moderate and five minutes of deep respiration. Levine tube in lower part of esophagus.

respiration 2.32 times as much air was aspirated as during the same period of normal respiration.

C. Clinical Case Studies.—1. A Case of Air Sucking: Mrs. N. A., a 38 year old housewife, presented a chief complaint of "attacks of belching" precipitated by "nervous excitement." In sequence her symptoms were excitement, dyspnea, abdominal distention and substernal or epigastric pain followed by rapid eructations of a nonoffensive gas. These eructations had occurred twenty to thirty times.

per minute, and during "attacks" they would continue from a few minutes to a whole day. Following the first attack, in 1938, the patient was hospitalized as a bed patient for six weeks because of the substernal pain which was attributed to coronary occlusion. Electrocardiographic studies failed to substantiate this diagnosis, and on return of symptoms the diagnosis was that she was "aerophagic," though swallowing was denied.

TABLE 7.—*Volume (Cc.) of Air "Aspirated" into Esophagus During Five Minute Periods of Respiration*

	Subject Number					Average Volume 1 Minute, Cc.
	1	2	3	4	5	
Normal respiration.....	26.1	.....	.....	194.2	361.8	39.5
Moderate respiration.....	297.5	132.6	120.2	.....	323.6	43.7
Deep respiration.....	241.2	544.7	643.1	265.3	603.0	91.9

This patient was observed fluoroscopically while she drank a half-glass of thin barium meal. The lumen of the esophagus appeared moderately widened but otherwise normal and initially only a small bubble of gas was visible in the stomach, as shown in figure 8 *A*. The patient, somewhat apprehensive, was then told that she was about to receive a rather painful treatment. This precipitated an "attack," and air immediately began to traverse the esophagus and enter the

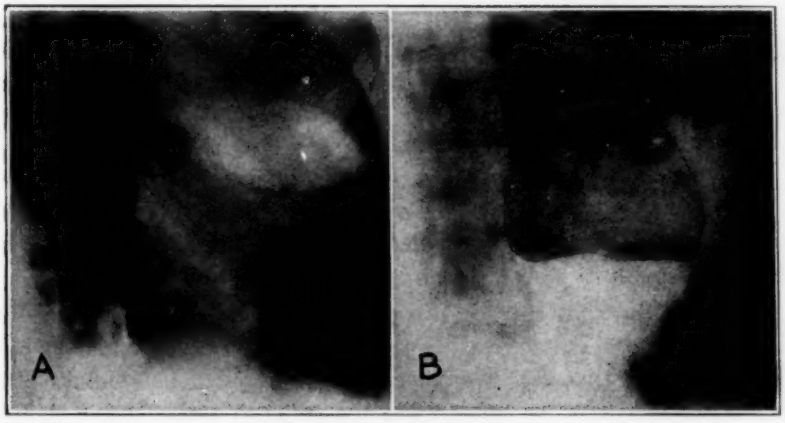

Fig. 8.—*A*, small gas bubble in stomach before air sucking. *B*, gaseous distention of fundus of the stomach in the same patient after thirty seconds of air sucking.

stomach. The diaphragm appeared to be relatively fixed during this process, and thoracic breathing predominated. In about thirty seconds appreciable gaseous distention of the fundus of the stomach had occurred, as shown in figure 8 *B*. Swallowing was not observed to occur, and peristalsis was apparent only as the last bit of air passed down the esophagus. This was thought to be a fairly typical example of gastric distention by air sucking.

2. A Case of Abdominal Distention: Mr. C. H., 73 years old, was hospitalized for a fractured femur incurred during a fall. The leg had been put up in traction, and when first observed by us the patient was somnolent, sleeping with his mouth

open and snoring loudly. He exhibited Cheyne-Stokes respiration, and pronounced abdominal distention had developed, though some flatus had been passed per rectum.

A Wangensteen continuous gastric suction was started, and a volumetric bottle was inserted in the system to measure the gas withdrawn. During the subsequent four hours 1,000 cc. of gas was aspirated from the stomach, without any apparent effect on the degree of distention. No true swallowing was noted during the time that could account for entry of the volume of gas withdrawn. However, it was observed that at irregular intervals the patient's tongue seemed to fall back in the throat, obstructing respiration. At the same time respiratory efforts continued, the thorax "jerking" rhythmically on inspiration. Almost simultaneously with these efforts from 10 to 30 cc. of gas returned through the Wangensteen apparatus.

This patient seemed to be using the mechanism of air sucking. With his jaw and throat relaxed he was making inspiratory efforts against a laryngeal obstruction. His distention could be explained on the basis of an "aspiration" of a greater volume of air than could be readily absorbed or expelled.

COMMENT AND SUMMMARY

Enormous abdominal distention occasionally occurs so rapidly that exogenous air is the only feasible source of the distending gas. The means, however, whereby air gains access to the upper part of the alimentary tract in such acute distention has not been definitely established, though air swallowing is generally assumed to be the mechanism involved. While in the vast majority of cases no definite observations on air swallowing are reported in the literature, in several instances extensive acute distention has been observed to occur in the absence of true swallowing. In an attempt to learn how this occurs conditions in which air is thought to gain entrance to the upper part of the alimentary tract without apparent swallowing have been reviewed. Of significance among these are acute dilatation of the stomach, air sucking and esophageal speech.

For experimental purposes acute dilatation of the stomach was selected as a representative entity amenable to study. Available information indicated that in this disease large or tremendous volumes of gas not infrequently have accumulated in the stomach within a few minutes. When accurate observations have been recorded swallowing was not noted to be the means of air entry; in fact, in a few cases a definite statement to the effect that swallowing did not occur has been made. A review of the etiologic precursors and proposed hypotheses of the mechanism in this disease provided no adequate explanation for its occurrence, but the acute onset and the wide variety of etiologic factors strongly suggested a reflex nervous mechanism. In the light of present day knowledge of extrinsic gastric innervation either reflex vagal inhibition or splanchnic stimulation could conceivably be implicated. Though seldom considered of significance the possible role of abnormal respiration as a factor in the distention mechanism deserves consideration,

for powerful respiratory efforts have occasionally been observed during the period of accumulation of gas.

All attempts to produce acute dilatation of the stomach in dogs by previously reported means failed. Likewise, experiments on animals devised on the basis of conditions which had supposedly led to acute distention in clinical cases met with no consistent success. In 3 of 17 dogs subdiaphragmatic vagal stimulation resulted in appreciable distention within thirty to sixty seconds, and though the source of gas or mechanism of transport could not be definitely determined, true swallowing was not observed.

Air sucking, a common practice in many normal persons who have learned to belch at will, might account for the means of air entry in acute distention. Its similarity to the mechanism employed for the intake of air by patients learning esophageal speech has been noted. In both instances decreased tone of the superior esophageal sphincter coincident with inspiration accounts for the ingress of air into the esophagus. Though not generally recognized, this sphincter normally excercises the important function of preventing air from entering the upper gastrointestinal tract during respiratory movements. By intubating this structure with a tube containing a one way valve gastric distention can be easily produced in anesthetized dogs. Application of a variety of stimuli that might reflexly inhibit the tone of the superior esophageal sphincter in animals proved essentially unsuccessful. However, in 7 of 17 dogs subjected to subdiaphragmatic vagal stimulation with faradic current pronounced fluctuations in sphincter tone were recorded, though complete isolation of this response from concurrent hyperpnea was not established. Current studies on the innervation of the esophagus indicate that in the dog motor innervation of the cervical third is principally through a single nerve, which may also have a direct effect on the motor activity of this sphincter.

Negative pressures developed in the upper alimentary tract during inspiration against a closed glottis were studied to determine their possible effectiveness in "aspirating" air if the superior esophageal sphincter were to relax. It was found that in human beings appreciable negative intragastric as well as intraesophageal pressures develop during inspiration against a closed glottis. This would seem to indicate that air could be aspirated right into the stomach if it be assumed that the superior esophageal and cardiac sphincters would not obstruct its entrance.

To determine whether significant volumes of air could be taken into the upper part of the alimentary tract without swallowing, 5 students who could perform "air sucking" were studied. It was found that the volume of gas "aspirated" into the stomach by air sucking was sufficient to account for enormous distention in a comparatively short time. Three "non-air-suckers" with their superior esophageal sphincter

intubated with a Levine tube also "aspirated" significant volumes of air by inspiration against a closed glottis. In fact, merely forceful respiration caused air to enter the esophagus and accumulate in the stomach when the superior esophageal sphincter was intubated and a one way valve prevented escape of this air on expiration. In view of these findings it seems reasonable to suggest that without swallowing some reflexly induced valvelike action of the superior esophageal sphincter might conceivably account for the means of entry of air in acute distention.

Although no unequivocal solution to the mechanism of acute distention has been reached by these studies, it appears likely that in cases in which actual swallowing is not observed air sucking may be the mechanism involved. What keeps every one from sucking air is the resistance offered by the superior esophageal sphincter, and one might postulate that general debilitation, anesthesia or some reflex may decrease the tone of this structure and allow significant volumes of air to enter the upper part of the gastrointestinal tract. The possible role of respiration in such a mechanism has also been mentioned.

CONCLUSIONS

1. Considerable evidence in the literature has established the fact that atmospheric air usually constitutes the largest percentage of distending gas in acute intestinal obstruction.

2. To determine how air gains entrance to the gastrointestinal tract through the esophagus there is need for more accurate observations on patients with acute abdominal distention, with evaluation in particular of the commonly accepted role of air swallowing.

3. Comparatively large negative intragastric as well as intraesophageal pressures develop during inspiration against a closed glottis.

4. Normally the superior esophageal sphincter prevents air from entering the upper alimentary tract without swallowing.

5. By voluntarily relaxing the tone of this sphincter and inspiring against a closed glottis air suckers and patients learning esophageal speech can "aspirate" air into the esophagus and stomach.

6. The volume of air that can be "aspirated" by air suckers, and by "non-air-suckers" whose superior esophageal sphincter is intubated, is considerable.

7. In disease, during anesthesia or as a result of a reflex, a decrease in tone of the superior esophageal sphincter might readily allow the entrance of exogenous air into the upper gastrointestinal tract without swallowing. Increased negative intraesophageal and intragastric pressures developed during abnormal respiration might well be an added factor in such a mechanism.

(Dr. A. C. Ivy) University of Illinois, Chicago.

SYMPOSIUM ON PEPTIC ULCER

EFFECT OF ENTEROGASTRONE ON MANN-WILLIAMSON ULCERS IN DOGS

H. C. SALTZSTEIN, M.D.

DAVID J. SANDWEISS, M.D.

JOHN M. HAMMER, M.D.

EDWARD J. HILL, M.D.

AND

HENRY J. VANDENBERG Jr., M.D.

DETROIT

THIS study has been conducted to evaluate the effect of orally administered enterogastrone on a series of dogs in which jejunal ulcer had been produced by the Mann-Williamson operation. Previous study of a similar nature by others [1] has shown that enterogastrone exerts a prophylactic, therapeutic and "immunizing" effect on the experimental Mann-Williamson ulcer when administered parenterally and orally. Recently Ivy and associates [2] reported a beneficial effect from enterogastrone in preventing recurrence of ulcer in the treatment of patients.

Enterogastrone is a hormone prepared from small intestine mucosa and exerts an inhibiting (or chalonic) effect on gastric motility and secretion. First prepared by Kosaka and Lim [3] from the mucosa of

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From the Research Division, Harper Hospital.

Presented at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 22, 1947.

1. Hands, A. P.; Greengard, H.; Preston, F. W.; Fauley, G. B., and Ivy, A. C.: Prevention of Experimental Gastrojejunal Ulcer by Enterogastrone Therapy, Endocrinology **30**:905 (June) 1942. Greengard, H.; Hands, A. P.; Grossman, M. I., and Ivy, A. C.: The Preparation of a Subcutaneously Effective Enterogastrone Concentrate, Federation Proc. **2**:17 (March) 1943. Hands, A. P.; Greengard, H.; Fauley, G. B., and Ivy, A. C.: Prevention of Experimental Gastrojejunal Ulcer by Enterogastrone, ibid. **2**:18 (March) 1943. Ivy, A. C.: The Prevention of Recurrence of "Peptic" Ulcer: An Experimental Study, Gastroenterology **3**:443 (Dec.) 1944.

2. Greengard, M.; Atkinson, N.; Grossman, M. I., and Ivy, A. C.: The Effectiveness of Parenterally Administered "Enterogastrone" in the Prophylaxis of Recurrences of Experimental and Clinical Peptic Ulcer, Gastroenterology **7**:625 (Dec.) 1946.

3. Kosaka, T., and Lim, R. K. S.: Demonstration of the Humoral Agent in Fat Inhibition of Gastric Secretion, Proc. Soc. Exper. Biol. & Med. **27**:890 (June) 1930.

the small intestine of dogs, it was subsequently prepared in purer form by Gray, Bradley and Ivy [4] from the mucosa of small intestine of hogs.

METHOD

The routine Mann-Williamson operation, as reported in a separate publication,[5] was performed on all animals. Intravenous pentobarbital sodium anesthesia was used. Silk suture material and open type anastomosis were routinely employed. Enterogastrone tablets, 0.5 mg., obtained through the courtesy of the Abbott Laboratories, were given orally, 8 tablets (4 Gm.) daily, starting one or two days postoperatively and continuing until the date of death of the animal. Diet consisted of hospital left-over food, principally meats, without vitamin or other supplements. A previously reported control series of 28 dogs on which the Mann-Williamson operation has been done [6] was used as a basis for comparison with the present study.

TABLE 1.—*Enterogastrone Series: Incidence of Ulcer and Survival Time*

	Dogs	Died	Ulcers	No Ulcers	Average Days After Operation	Dogs Still Alive After Operation
Control	28	28	28	0	71	0
Mann-Williamson operation, enterogastrone	15	14	11	3	96 plus	1*

* Alive 259 days on April 20, 1947. See footnote at bottom of table 3.

RESULTS

Fifteen dogs, including both sexes, comprised the enterogastrone series. Fourteen dogs have died with average survival time of 84.4 days. Including the 1 living dog the average survival time is 96 days at the time of the report, compared with 71 days for the control series (table 1).

In the enterogastrone-treated series the longest survival time is 259 days (compared with 135 days in the control group); the shortest survival time was 25 days (compared with 13 days for the control group).

Eleven of the enterogastrone-treated dogs died with jejunal ulcers, (with an average survival time of 97 days). The ulcers were located

4. Gray, J. S.; Bradley, W. B., and Ivy, A. C.: On Preparation and Biological Assay of Enterogastrone, Am. J. Physiol. **118**:463 (March) 1937.

5. Saltzstein, H. C.; Sandweiss, D. J.; Hammer, I. M.; Hill, E. J., and Vandenberg, H., Jr.: Effect Vagotomy on Mann-Williamson Ulcer in Dogs, Arch. Surg., this issue, p. 130.

6. Beaver, D. C.; Sandweiss, D. J.; Saltzstein, H. C.; Farbman, A. A., and Sanders, A. W.: Effect of Urine Extracts on Prevention and Healing of Experimental Ulcers in Dogs, Am. J. Clin. Path. **12**:617 (Dec.) 1942.

in the jejunum opposite the gastroenterostomy stoma, in the direct line of flow of gastric contents. Grossly, the ulcers varied in diameter from 0.5 cm. to 6.0 cm. One animal showed three ulcers. In the remainder, only one ulcer was present. Jejunitis was not observed in any of the dogs. Ulcers of 4 of the animals were examined microscopically. They failed to show epithelization, but in all there was a varying degree of fibroblastic and vascular proliferation of the ulcer base which did not vary significantly from that observed in the control series.

Of the 11 dogs with jejunal ulcer, 10 had perforated ulcers, generalized peritonitis accounting for death. The ulcer in the eleventh animal was superficial, the animal dying from pneumonia. Three dogs died without ulcer (with an average survival time of 38 days). The cause of death in those animals is shown in table 2.

The 1 living dog in the enterogastrone series (259 days of postoperative survival) went through a successful pregnancy during treatment, which might have had some beneficial effect (on its survival time)

TABLE 2.—*Enterogastrone Series: Survival and Causes of Death in Dogs Without Ulcer*

Dog	Days After Operation	Cause of Death
1	60	Cachexia
2	30	Peritonitis
3	25	Intestinal obstruction; intussusception

for peptic ulcer in women has been shown to be relieved and benefited during gestation.[7] (Also see footnote at bottom of table 3.)

COMMENT

In the present series some benefit from the oral administration of enterogastrone was observed. Three (21 per cent) of 14 dogs did not experience ulcer as compared with the presence of ulcer at autopsy in all of the 28 dogs in the control series.

Three of the animals that died with ulcer lived longer than the maximum survival time of our control animals (i. e., 186, 180 and 256 days). One of the enterogastrone-treated animals is still alive and in good condition two hundred and fifty-nine days after the Mann-Williamson operation. (See footnote at bottom of table 3.)

The incidence of ulcers (79 per cent) and average survival time of 96 days in the present series compare unfavorably with results of a

7. Sandweiss, D. J.; Saltzstein, H. C., and Farbman, A. A.: Prevention or Healing of Experimental Peptic Ulcer in Mann-Williamson Dogs with Anterior Pituitary-Like Hormone (Antuitrin S): Preliminary Report, Am. J. Digest Dis. **5**:24 (March) 1938.

similar series reported by Ivy.[8] The fact that the diet in our series was not supplemented by pancreas or raw liver may have contributed to the comparatively short survival time. However, our control series did not receive these supplements in their diet. It is also possible that the enterogastrone used by Ivy, and prepared in his own laboratory, might have been more potent. However, the commercial product fed our dogs was prepared by the same method and under Dr. Ivy's direction. If the difference in our results should be explained by variation in potency, then indeed, the present method of preparing enterogastrone and the present method of assaying the potency of the product need immediate reevaluation if it is to be used therapeutically on patients with ulcers.

TABLE 3.—*Enterogastrone Series: Summary of Results*

Dog	Survival Time, Days	Ulcer		Cause of Death
		Appearance	Measurements	
1 (dog 2, table 2)	30	None	.....	Peritonitis
2	89	Perforated	3 mm. diameter	Peritonitis
3	88	Perforated	3 x 5 cm.	Peritonitis
4	56	Superficial	1 cm.	Pneumonia
5 (dog 1, table 2)	60	None	.....	Cachexia
6	52	Perforated	1 x 1 cm.	Peritonitis
7	175	Perforated	5 x 3 cm.	Peritonitis
8	33	Perforated	3 ulcers 0.5 x 0.5 cm.	Peritonitis
9	73	Perforated	1 x 1 cm.	Peritonitis
10 (dog 3, table 2)	25	None	.....	Intussusception
11	30	Perforated	1 cm. diameter	Peritonitis
12	35	Perforated	1 x 1.5 cm.	Peritonitis
13	256	Perforated	1.5 x 1.5 cm.	Peritonitis
14	180	Perforated	2 cm. diameter	Peritonitis
15	259*	(4/20/47) Still alive	.....	.....
Average (exclusive of dog 15)	84.4	No ulcer: 3		
Average (inclusive of dog 15)	96	Perforated: 10 Superficial: 1 Still alive: 1		

* An exploratory operation was performed 389 days after operation. The upper gastroenterostomy stoma was clean and smooth, and there was no ulcer or induration. However, the lower anastomosis was found to have been made 22 inches (55.8 cm.) from the ileocecal valve instead of the routine 10 to 12 inches (25 to 30 cm.), and this might have been responsible, at least in part, for the prolonged postoperative survival time and the absence of an ulcer at the time of the exploratory operation.

SUMMARY

The effect of orally administered enterogastrone in a series of 15 dogs on which the Mann-Williamson operation had been done was studied. Results were compared with a previously conducted control series of 28 dogs.

Survival time of the enterogastrone-treated series is 96 days while that of the control series was 71 days.

Twenty-one per cent (3 dogs) of the enterogastrone-treated series did not have ulcer; there was an average survival time of 38 days for this

8. Ivy, A. C.: The Problem of Peptic Ulcer, J. A. M. A. **132**:1053 (Dec. 28) 1946.

group. Of the 79 per cent (11 dogs) that died with ulcer (average survival time 97 days) 10 had perforated ulcers. In the control series, all the dogs showed ulcer at autopsy, and 72 per cent of the ulcers were perforated.

Three of the enterogastrone-treated animals that died with ulcers lived longer than the maximum survival time of our control dogs: 175, 180 and 256 days. One of the treated dogs is still alive and in good condition 259 days after the Mann-Williamson operation. (See footnote under table 3.)

The results of this study show that some beneficial therapeutic effect on experimental Mann-Williamson ulcers in dogs was obtained by the oral administration of enterogastrone.

EFFECT OF VAGOTOMY ON MANN-WILLIAMSON ULCERS IN DOGS

H. C. SALTZSTEIN, M.D.
DAVID J. SANDWEISS, M.D.
JOHN M. HAMMER, M.D.
EDWARD J. HILL, M.D.
AND
HENRY J. VANDENBERG Jr., M.D.
DETROIT

THE PRESENT study was conducted for the purpose of determining the effect of vagotomy on experimentally produced Mann-Williamson peptic ulcers in dogs. Although there are other methods of experimentally producing peptic ulcers, the Mann-Williamson operation was chosen because the jejunal ulcer which ensues closely simulates the postoperative jejunal ulcer seen in man. In 98 to 100 per cent of control animals jejunal ulcers develop after the operation.

METHOD OF STUDY

The Mann-Williamson operation was performed in the standard manner, viz: transection at the pylorus, closure of the duodenal stump, transection of the jejunum 4 inches (10.1 cm.) beyond Trietz' ligament, end to side gastrojejunostomy using the distal cut portion of the jejunum and side to side jejunoileostomy anastomosing the proximal cut portion of the jejunum to the ileum 25 cm. above the ileocecal valve (fig. 1). This short-circuits the bile, pancreatic juice and duodenal secretions into the terminal ileum. Ulcers nearly always form directly opposite the gastroenterostomy stoma. The short-circuiting of the upper segment of the small bowel causes nutritional disturbance resulting in loss of weight and frequently in diarrhea. Ivy [1] has obviated this by daily feedings of whole pancreas and liver. In the present study the diet consisted of hospital left-over food, principally meats, with no supplements, similar to the diet given to our control series.

Intravenously administered pentobarbital anesthesia was used, the average dose being 1 grain (0.06 Gm.) per 5 pounds (2.3 Kg.) of body weight. Endotracheal intubation was used in all cases. Surgical approach for vagotomy was made through the left seventh interspace. The trunks of the two main vagus nerves and any anastomosing branches were isolated in the immediate supradiaphragmatic region and a 1 to 2 inch (2.5 to 5 cm.) segment of the anterior and posterior vagi, with all visible branches, was removed. Oxygen was administered as necessary. The lungs were reexpanded before the chest wall was closed. In several cases the chest was aspirated postoperatively to determine the presence or absence of

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1. Ivy, A. C.: The Problem of Peptic Ulcer, J. A. M. A. **132**:1053-1059 (Dec. 28) 1946.

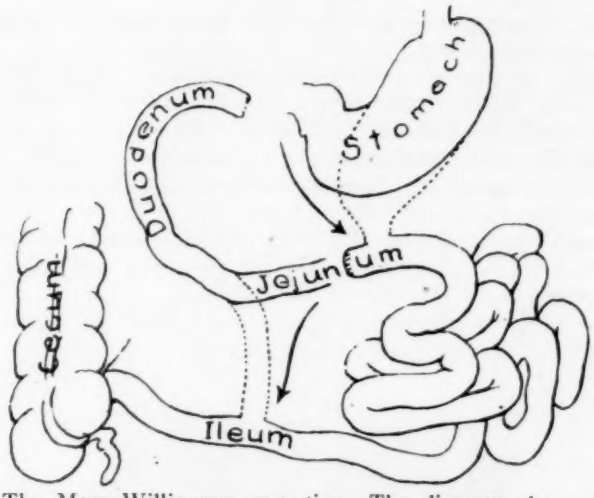

Fig. 1.—The Mann-Williamson operation. The diagram shows steps in the procedure: (1) transection of stomach at pylorus and closure of duodenal end; (2) end to side gastrojejunostomy utilizing upper part of jejunum, and (3) jejuno-ileostomy at 25 cm. above cecum.

Fig. 2 (dog 4).—Jejunitis of mild severity. Animal survived thirty-three days after vagotomy. The mucosa shows patchy reddening with some confluence. No ulcer is present.

pneumothorax and therapeutic aspirations were repeated daily as necessary. Usually one or two aspirations sufficed.

Vagotomy preceded the Mann-Williamson operation in 1 animal (table 1, dog 1). The postvagotomy gastric dilatation so frequently encountered made the Mann-Williamson operation more difficult to perform. Performing of the two procedures simultaneously was tried, but the animals withstood these operations poorly and only 1 survived long enough to be included in the series (table 1, dog 10). Vagotomy was performed after the Mann-Williamson procedure in 10 cases.

The average interval between the Mann-Williamson operation and vagotomy was eleven days. In compiling our results no animal was used unless it survived the second operation for a minimum of twelve days.

Preoperative care consisted of twenty-four hour fasting. No preoperative medication was given. Routine postoperative care following the Mann-Williamson

Fig. 3.—Severe jejunitis. The animal survived five days after vagotomy (therefore not included in the series). Note diffuse, marked reddening and thickening of mucosa, present in upper 25 cm. of jejunum.

operation consisted of administration of fluids orally for twenty-four hours, followed by a general diet. Five per cent dextrose in saline solution was occasionally given postoperatively, intravenously or subcutaneously during the first few postoperative days, when indicated. Following reaction from anesthesia after vagotomy the regular diet was resumed. Gastric aspiration was performed on 5 dogs (dogs 6 through 10, table 1). Aspiration was performed once daily for four days routinely and then discontinued unless the stomach contained abnormal amounts of food or fluid.

RESULTS

CONTROL MANN-WILLIAMSON ULCER SERIES

A previously reported series of 28 control dogs with Mann-Williamson ulcers has been used for comparison.[2] All of these ani-

mals died with typical jejunal ulcers; the average survival time was seventy-one days following operation (minimum thirteen days and maximum one hundred and thirty-five days.) Seventy-two per cent of the animals died of peritonitis following perforation of an ulcer. Only two of the ulcers showed attempts at healing. There was no evidence of jejunitis or gastric dilatation in any of the cases.

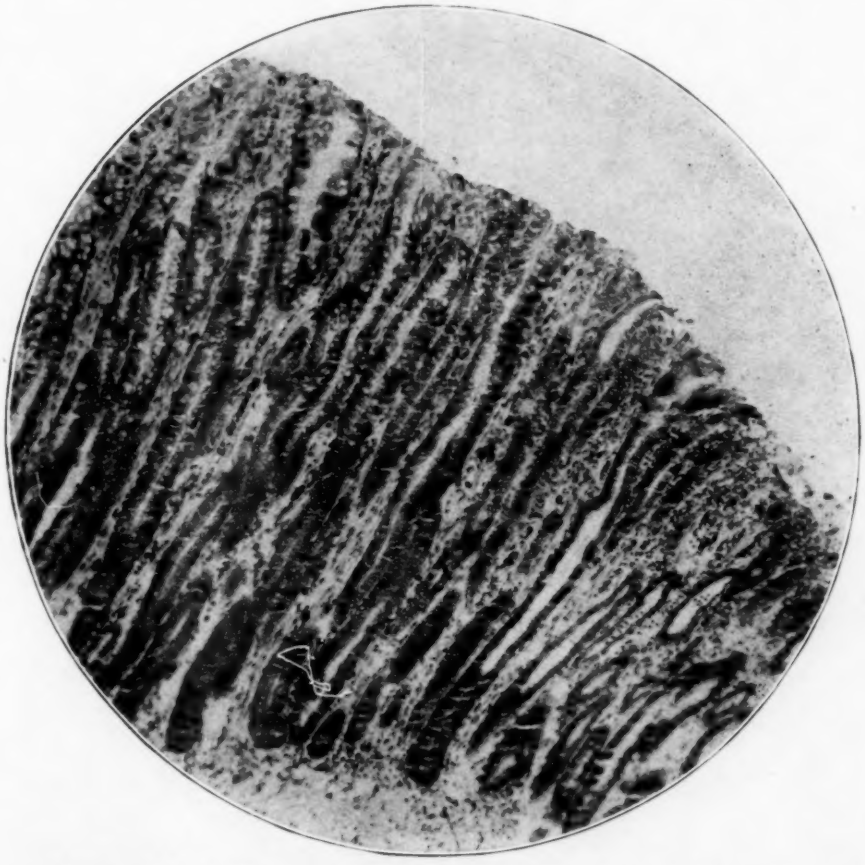

Fig. 4.—Normal jejunum of dog showing mucosa. Note regular arrangement and length of villi. ×125.

MANN-WILLIAMSON–VAGOTOMY SERIES

In this series 12 dogs survived the Mann-Williamson operation nineteen days or longer, and the vagotomy operation twelve days or longer. These 12 dogs comprise our series.

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2. Beaver, D. C.; Sandweiss, D. J.; Saltzstein, H. C.; Farbman, A. A., and Sanders, A. W.: Effect of Urine Extracts on Prevention and Healing of Experimental Ulcers in Dogs, Am. J. Clin. Path. **12**:617-629 (Dec.) 1942.

1. *Postoperative Survival Time.*—The survival time was considerably shorter in the vagotomized series than in the control series, being fifty-one days following the Mann-Williamson operation (forty-four days following vagotomy) compared to seventy-one days for the control series.

2. *Mann-Williamson Ulcers.*—Jejunal ulcers were found in 6 of the 12 animals (table 1). Of greater significance, however, is the fact

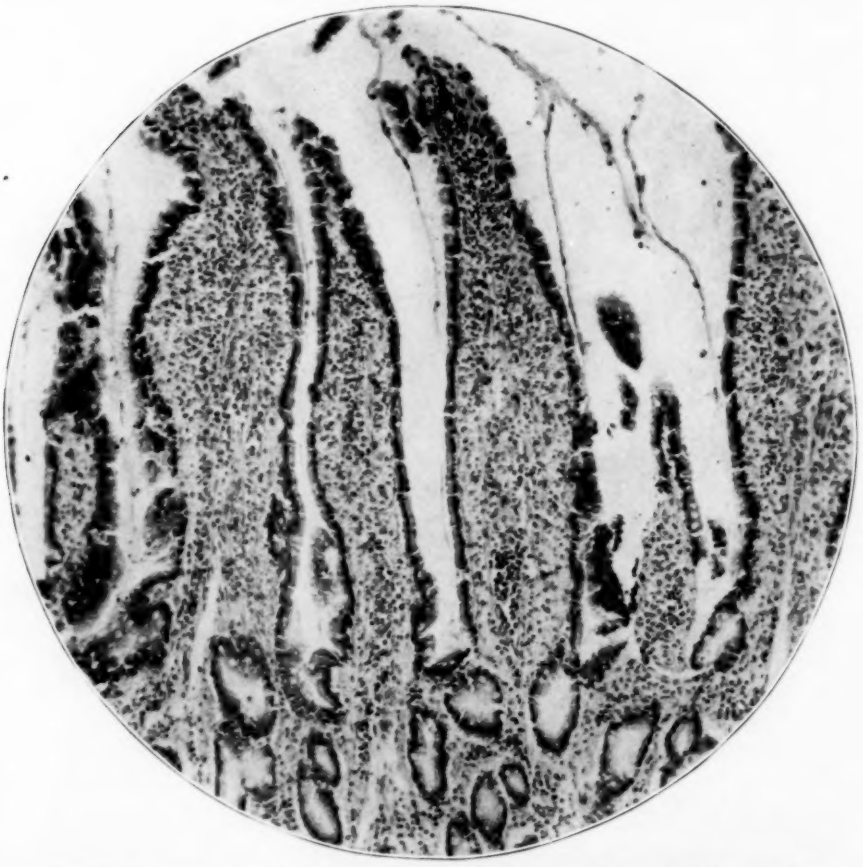

Fig. 5.—Severe jejunitis in dog after vagotomy and Mann-Williamson operation. Note thickening and increased length of villi with cellular infiltration. Under same magnification as figure 4; × 125.

that of the 8 animals that lived more than one month after the Mann-Williamson operation (twenty-four days after vagotomy) 6 were found to have ulcers.

In previous experience, if any substance or method had a prophylactic or therapeutic effect on Mann-Williamson ulcers, it was more evident the longer the dog survived; i. e. some of the ulcers which

routinely develop after one or two months were prevented or healed, or the survival time of the animal was prolonged. These beneficial effects were not observed after vagotomy.

Of the 6 animals that died with ulcer, in 2, a single small superficial ulcer was present. Two others had penetrating ulcers (one 0.5 cm. in diameter, the other 3.0 cm. in diameter.) One had three ulcers (each measuring 1 cm. in diameter, one perforated, one penetrating and one superficial). The last dog had an ulcer which was 2 cm. in diameter and had perforated.

TABLE 1.—*Series of Dogs on Which the Operation and Vagotomy Were Performed*

Dog	Survival Mann-Williamson Operation, Days	Survival Vagotomy, Days	Dilatation 0 to —	Ulcer		Jejunitis 0 to —
				Type	Diameter	
1*	157	182	— — —	Penetrating	3.0 cm.	— — —
2	50	43	— — —	Superficial	0.5 cm.	0
3	34	24	0	Perforated	3.5 cm.	— — —
4	38	33	— —	None	.....	— —
5	50	28	—	Superficial	1.0 cm.	—
6	66	38	0	Penetrating	0.5 cm.	0
7	61	74	0	None	.....	0
8	19	12	—	None	.....	— —
9	25	17	— —	None	.....	— —
10†	47	47	— —	Perforated	1.0 cm.	0
				Penetrating	1.0 cm.	0
				Superficial	1.0 cm.	0
11	19	14	—	None	.....	— —
12	21	16	— — —	None	.....	0
Average	51	44				
Totals			Dilatation —9 None 3	Ulcer—6 No ulcer—6		Jejunitis—7 None—5

* Vagotomy performed twenty-five days before Mann-Williamson operation. Vagotomy did not prevent ulcer formation.

† Mann-Williamson operation and vagotomy performed simultaneously. Vagotomy did not prevent formation of ulcer.

Note:—Four of the 6 dogs that died without ulcer lived on the average only twenty-one days after the Mann-Williamson operation. It is possible that had these animals lived longer, typical ulcers might have developed as occurred in 6 of the remaining 8 animals with an average postoperative (Mann-Williamson) survival time of sixty-five days.

The ulcers of 4 of the animals were examined microscopically. Epithelization of the surfaces of the ulcer was not observed. The surfaces were necrotic, with varying numbers of cells of acute and chronic inflammation. Fibroblastic and vascular proliferation of the base was present in all cases in considerable degree but the appearance did not differ appreciably from that found in the previously reported control series.[2]

It is of interest to note that in 1931, Beaver and Mann[3] reported results on 3 control dogs with Mann-Williamson ulcers, 3 dogs with Mann-Williamson ulcers with splanchnic nerve resection and 3 dogs with Mann-Williamson ulcers and supradiaphragmatic vagotomies. In all the typical jejunal ulcers developed with the exception of 1 in the latter

3. Beaver, M. G., and Mann, F. C.: The Production of Peptic Ulcer After Section of the Gastric Nerve, Ann. Surg. **94**:1116-1118 (Dec.) 1931.

group. They concluded that "Section of nerves to the stomach did not prevent the development of ulcer in that portion of the intestines which received the gastric content after measures had been taken to drain the duodenal secretion away from that region."

3. *Jejunitis in the Vagotomized Animals.*—In 7 of the 12 dogs jejunitis of varying severity was present. It was located in the upper

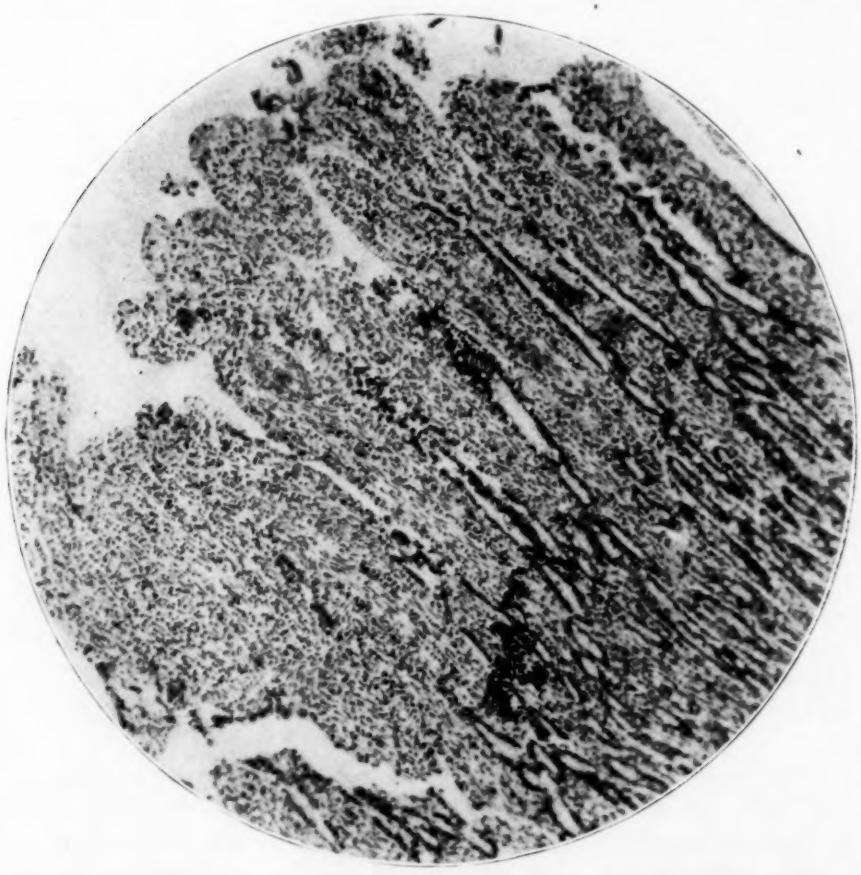

Fig. 6.—Jejunitis in dog after vagotomy and Mann-Williamson operation. Note edema, hyperemia and cellular infiltration of terminal villi. More normal villi near base. × 125.

part of the jejunum, usually confined to the upper 14 inches (35.5 cm.) or less. The most extensive area of involvement was 18 inches (45.7 cm.). Its minimal manifestation was a patchy mucosal reddening, for several inches beyond the anastomosis (see fig. 2). Its maximum manifestation was a diffuse reddening and carpet-like thickening

and hypertrophy of the mucosa, most severe in the upper portion, beginning immediately at the gastrojejunostomy anastomosis and gradually tapering off distally (see fig. 3). Analysis of the 7 cases reveals that in 2 cases the jejunitis was diffuse and severe for 18 inches and 14 inches respectively. In 4 cases it was of moderate severity. In 1 case it was scattered and mild, the intensity of redness being less marked than in the other observed cases. No correlation with

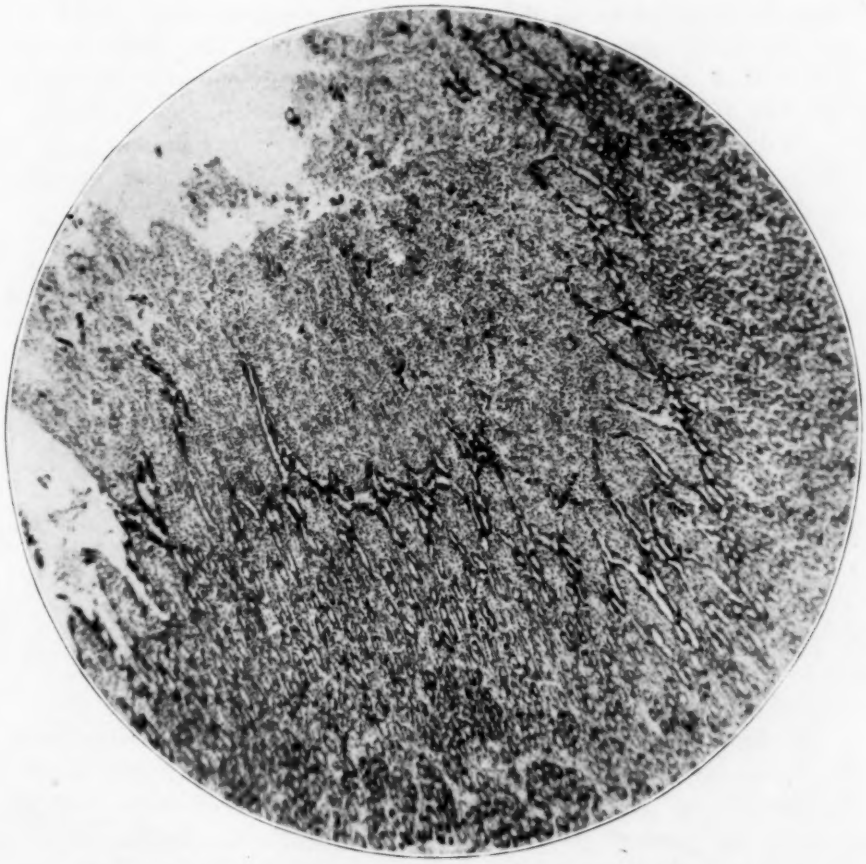

Fig. 7.—Jejunitis in dog after vagotomy and Mann-Williamson operation. The mucosa is about twice the normal thickness, with terminal villi as described in figure 6. × 75.

survival time was observed. The 2 severe cases were present in dogs with survivals of one hundred and eighty-two and twenty-four days after vagotomy. The cases of moderate jejunitis occurred in dogs with survivals of thirty-three, seventeen, fourteen and twelve days, the average time of survival being nineteen days. The mild case was in a dog that survived twenty-eight days.

Microscopically, there were marked hypertrophy and edema of the villi, engorgement and proliferation of capillaries and especially in the free ends of the villi. There were subacute inflammation with infiltration of round cells and a smaller number of polymorphonuclear leukocytes (figs. 4, 5, 6 and 7).

Of the 6 dogs with jejunal ulcers severe jejunitis was present in 2, and it is worthy of note that both of these cases represented dogs with the largest ulcers in the series, one a 3.5 cm. diameter ulcer which perforated causing death on the twenty-fourth postoperative day and the other a 3 cm. ulcer which had penetrated deeply. The latter animal survived one hundred and eighty-two days, the only one in which vagotomy was done before the Mann-Williamson operation.

Of the 5 remaining cases of jejunitis no ulcer was present in 4 of the dogs having moderately severe jejunitis. In the case of mild jejunitis a superficial ulcer 1 cm. in diameter was present.

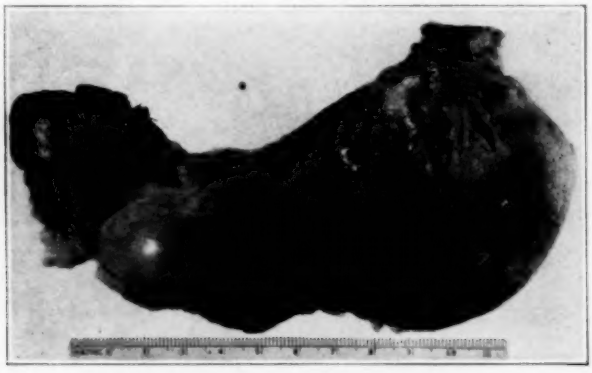

Fig. 8.—Normal stomach in dog that survived one day after Mann-Williamson operation.

As stated, 7 of our 12 vagotomized dogs that had Mann-Williamson ulcers were found to have jejunitis of varying severity. Based on our experience with over 350 dogs with Mann-Williamson ulcers used as controls and treated with various medicaments, the finding in our laboratory of jejunitis in 60 per cent of our vagotomized dogs that had Mann-Williamson ulcers is definitely significant.

4. *Gastric Dilatation.*—Gastric dilatation was present at autopsy in 9 of the 12 dogs (75 per cent) (figs. 8 and 9). It was usually a saccular dilatation, involving only the fundus and body of the stomach, with the antrum contracted and tubelike. Table 2 shows the degree of dilatation and the correlation with postoperative survival time.

Table 2 shows that gastric dilatation was most frequently found in animals surviving for the shortest time, in that 5 of the 9 cases were

in animals that survived less than one month. However, 1 dog showed marked dilatation one hundred and eighty-two days after vagotomy.

TABLE 2.—*Gastric Dilatation*

Degree of Dilatation	Number of Dogs	After Vagotomy, Survival Time		
		0-30 Days	30-60 Days	Over 60 Days
Marked	3*	1	1	1
Moderate	3	1	2	..
Mild	3	3	..	..
Totals	9	5 (Av. 17 days)	3 (Av. 41 days)	1 (182 days)

* Cause of death in 2 cases.

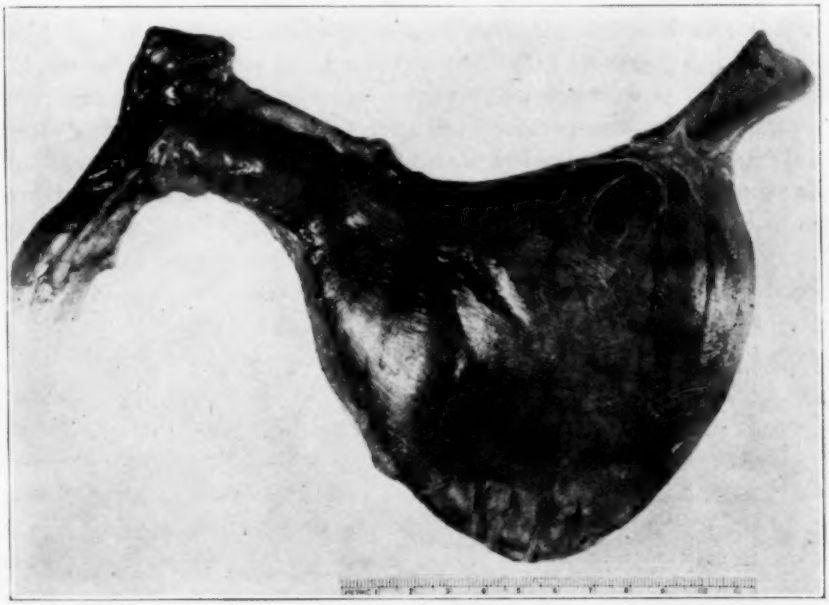

Fig. 9.—Gastric dilatation of type frequently seen after Mann-Williamson operation and vagotomy. Note pouchlike dilatation of fundus and contraction of antrum.

SUMMARY

Twenty-eight control dogs survived the Mann-Williamson operation an average of seventy-one days. Twelve dogs on which vagotomy plus the Mann-Williamson operation was performed survived a much shorter time, i. e., fifty-one days after the Mann-Williamson operation and forty-four days after vagotomy. Of the controls, 100 per cent showed ulcer at autopsy; 72 per cent of these died of perforation with peritonitis. Of the vagotomized animals, in 6 of the 8 that lived more than one month after the Mann-Williamson operation jejunal ulcers developed.

An inflammatory reaction of varying severity was found in the upper part of the jejunum in 7 of 12 dogs on which Mann-Williamson operations and vagotomy were performed. There was no correlation with survival time. Gastric dilatation was present in 9 of the 12 dogs. This occurred more frequently in dogs with short survival time, but 1 animal showed marked gastric dilatation one hundred and eighty-two days after vagotomy. (The vagotomy was done twenty-five days before the Mann-Williamson operation.)

CONCLUSIONS

The postoperative survival time of dogs on which the Mann-Williamson operation and also transthoracic vagotomy were performed was much shorter than that of the control animals. In 6 of 8 dogs on which both operations were done and which lived one month ulcer developed. Gastric dilatation was present in 75 per cent of the vagotomized dogs, most frequently in those of short survival. Jejunitis of varying severity was present in 60 per cent of the vagotomized dogs.

If such jejunitis should be found to exist in patients after vagotomy, it might explain the diarrhea which at times follows this surgical procedure.

SECTION OF THE VAGUS NERVES TO THE STOMACH IN THE TREATMENT OF BENIGN GASTRIC ULCER

PAUL V. HARPER Jr., M.D.
AND
LESTER R. DRAGSTEDT, M.D., Ph.D.
CHICAGO

DURING the past four years, section of the vagus nerves to the stomach as a method of treatment has been carried out at the University of Chicago in 250 patients with various types of peptic ulcer. The technics employed have been described elsewhere.[1] The clinical results following this method of treatment have been so satisfactory that it has replaced all other types of surgical treatment for this disease on our service. One patient in this series died of pneumonia, making a mortality of 0.4 per cent. Physiologic tests on 170 patients on whom the operation was performed by us have revealed that the section of the vagus nerves was probably incomplete in 18 cases. In this group, 6 patients have complained of recurrent or persistent symptoms of ulcer, and in 2 of these an undamaged vagus fiber was found at a second operation. Division of this nerve was followed by complete relief. The remaining 164 patients have remained free from all types of ulcer distress on an entirely unrestricted diet and without medication. The side effects of section of the vagus nerves, such as symptoms of delayed gastric emptying and diarrhea, which have been discussed elsewhere, have proved to be transitory and, on the whole, inconsequential. The operation was performed by the transthoracic approach in 61 patients and by the transabdominal route in 109 patients. It was combined with gastroenterostomy in 71 patients, and in 5 patients with cicatricial obstruction at the pylorus a subsequent gastroenterostomy was required. The operation was performed in 147 patients for duodenal ulcer, in 15 patients with gastrojejunal ulcer and in 8 patients with gastric ulcer. The present paper is concerned with the latter group.

From the Department of Surgery of the University of Chicago.

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Read at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 22, 1947.

1. Dragstedt, L. R., and Shafer, P. W.: Removal of the Vagus Innervation of the Stomach in Gastroduodenal Ulcer, Surgery **17**:742-749 (May) 1945.

While there is no reason to believe that the pathogenesis of gastric ulcer is in any way different from that of ulcer of the stomach or jejunum, the possibility of cancer in the former case makes it an entirely different and special surgical problem. When the lesion is in the pyloric antrum and readily accessible, it is probably best treated by a subtotal gastrectomy. This operation can now be performed with a negligible mortality. A recurrent gastrojejunal ulcer is rare following subtotal gastrectomy for gastric ulcer, although a definite hazard in cases of duodenal ulcer. If microscopic examination reveals that the lesion is malignant, a local removal has been accomplished and the diagnosis has been made, the advisability of further radical surgical treatment can be considered. When, however, the lesion is high on the lesser curvature close to the esophagus, a resection extensive enough to have any meaning for the treatment of a possible malignant growth would involve a total gastrectomy. This operation is much more hazardous than partial gastrectomy, and the resulting digestive and nutritive defect constitutes a definite disadvantage. When these facts are taken into consideration, together with the small percentage of gastric cancers that can be cured by any type of surgical treatment, a total gastrectomy is not justified in the absence of a definite diagnosis of malignant growth.

In the patient with a gastric ulcer and a coexistent active duodenal ulcer, the possibility of malignant growth is generally believed to be extremely small. There were 3 cases of this type in our series, all refractory to medical management. Following section of the vagus nerves to the stomach, the ulcers healed as demonstrated by fluoroscopic examination or gastroscopy. Healing took place within two weeks in 1 case, and within four weeks in the remaining 2. These ulcers have not recurred, and the patients have remained free of ulcer distress without medication or any type of dietary restriction.

REPORT OF CASES

CASE 1.—A 38 year old police officer complained of intermittent attacks of typical ulcer distress for the preceding three years. Nine months before admission, he was operated on elsewhere for a perforated duodenal ulcer. On his admission, roentgen examination revealed ulcer craters in both the pyloric antrum and the duodenal bulb (fig. 1 *A*). Transthoracic section of the vagus nerves to the stomach was performed on May 3, 1947, and after this operation the patient has been free of distress without medication or dietary restriction. Roentgen examination on May 31 (fig. 1 *B*) revealed that both ulcers were healed. Nine months after the vagotomy, an episode of acute gastric distention occurred following the excessive ingestion of food. This was completely relieved by three days of gastric decompression.

CASE 2.—A 42 year old male office worker complained of epigastric distress refractory to medical management for the preceding eighteen months. Roentgen

examination (fig. 2 *A*) revealed two ulcer craters on the lesser curvature of the stomach, together with deformity of the duodenal bulb with a crater. At gastroscopy, two sharply punched out gastric ulcers, 1 and 1.5 cm. in diameter respectively, were visualized. Section of the vagus nerves with posterior gastroenterostomy was performed on Nov. 1, 1946. The epigastric pain was immediately relieved.

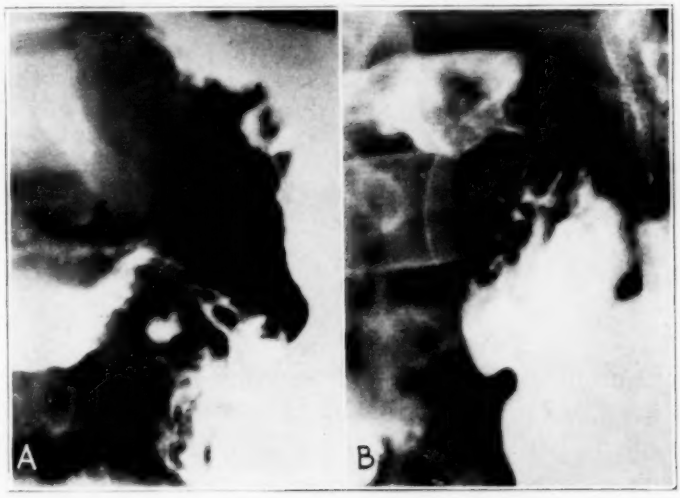

Fig. 1 (case 1).—*A*, roentgenogram showing large ulcer crater in the antrum. *B*, roentgenogram twenty-eight days after gastric vagotomy showing disappearance of crater in antrum.

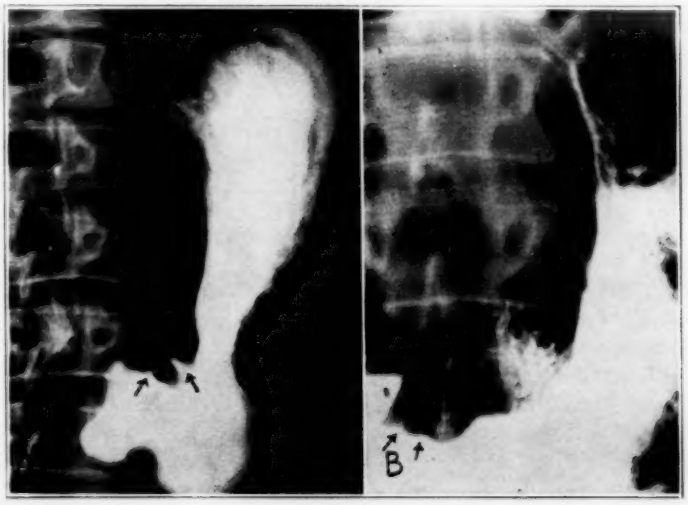

Fig. 2 (case 2).—*A*, roentgenogram showing two ulcer craters on the lesser curvature of the stomach. *B*, roentgenogram ten days after gastric vagotomy showing almost complete healing of the ulcers shown in *A*.

The typical distress was reproduced on November 2 and 3 by the installation of a solution of hydrochloric acid into the stomach (the Palmer acid test). On November 11 roentgen examination (fig. 2 *B*) revealed complete healing of the ulcers, and gastroscopic examination the following day confirmed this. The patient has remained entirely free of symptoms to the present.

CASE 3.—A 39 year old man, a streetcar conductor, complained of intermittent attacks of epigastric distress with occasional melena for the previous ten years. Roentgen examination revealed pronounced deformity of the duodenal bulb with crater and stiffness of the lesser curvature of the stomach with two small craters in this area. The gastric ulcers were visualized at gastroscopic examination. Section of the vagus nerves to the stomach with anterior gastroenterostomy was performed on Sept. 25, 1946, and at this operation, the interior of the stomach was inspected. The ulcers were readily seen and appeared benign. Gastroscopic examination on October 3 revealed that the gastric ulcers had healed, and roentgen examination on December 16 showed complete disappearance of the ulcer craters. The patient has remained free of ulcer symptoms and has a ravenous appetite.

In 3 of the patients in this series, large chronic gastric ulcers were present high on the lesser curvature of the stomach. These patients have been repeatedly examined over periods of two to four years in the medical department of this hospital with repeated fluoroscopic and gastroscopic studies. During this time, the ulcers had proved refractory to all types of medical management, including roentgen therapy to the stomach. Subtotal gastrectomy as a method of treatment had been refused. In all 3 cases, the ulcers healed promptly after section of the vagus nerves, and in 1 instance healing was apparent within a three week period as determined by roentgen examination. All these patients have remained well, 1 for over three years and 1 for over two years.

CASE 4.—A 46 year old male laborer was first seen in April 1941, at which time he gave a history of burning epigastric distress relieved by food for the previous two years. Roentgen examination was reported to reveal an ulcer high on the lesser curvature of the stomach. Resection of the stomach was advised but refused. Repeated gastroscopic and fluoroscopic examinations were made. On June 25, 1943, an ulcer 1 by 2 by 1.5 cm. was visualized at gastroscopy. Fluoroscopic examination at this time revealed the ulcer crater shown in figure 3 *A*. On July 7 a transthoracic section of the vagus nerves to the stomach was performed. The ulcer distress was promptly and entirely relieved, and the patient returned to his usual occupation. Gastroscopic examinations on Oct. 22 and Dec. 27, 1943, and March 27, June 5, Aug. 27, Nov. 6, 1944, and May 21, 1944, have revealed no recurrence of the previous ulcer. This has been confirmed by roentgen examination on Feb. 11, 1944 (fig. 3 *B*).

CASE 5.—A 43 year old male laborer has been treated in this clinic for diabetes mellitus since 1933. In May 1941 he experienced severe abdominal pain, and a gastric ulcer with a small perforation was diagnosed. The patient recovered on medical management. Later, the ulcer symptoms returned, and in spite of a diagnosis of possible malignant growth the patient refused gastric resection.

Repeated gastroscopic and roentgen examinations were made, and during this time the patient continued to have recurrent attacks of pain with associated vomiting. On March 1, 1945 a transthoracic section of the vagus nerves to the stomach was performed. On April 17 roentgen examination revealed no evidence of a crater, and this was confirmed on May 11, 1945, and June 9, 1946. Gastro-

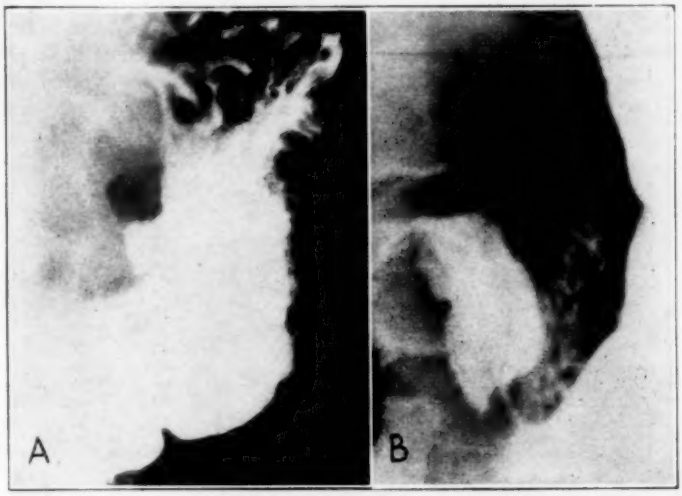

Fig. 3 (case 4).—*A*, roentgenogram showing a large ulcer crater on the lesser curvature of the stomach. *B*, roentgenogram showing complete healing of the ulcer shown in *A*, seven months after gastric vagotomy.

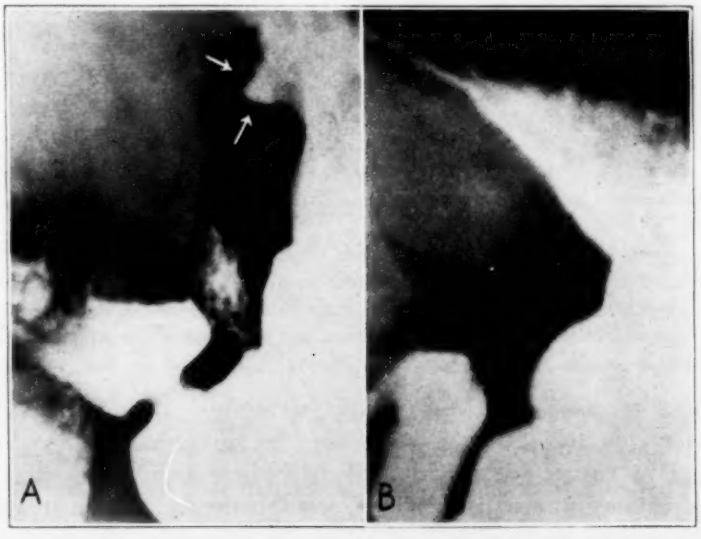

Fig. 4 (case 6).—*A*, roentgenogram showing a large ulcer crater high on the lesser curvature of the stomach. *B*, roentgenogram showing healing of ulcer shown in *A*, twenty-one days after gastric vagotomy.

scopic examination on May 18, 1945 revealed what appeared to be a benign gastric ulcer, and this had disappeared on reexamination by the gastroscope on September 7. This man has remained entirely well except for occasional attacks of diarrhea.

CASE 6.—A 46 year old machinist has complained of recurring attacks of epigastric pain relieved by food and alkali since April 1942. A gastric ulcer was demonstrated by roentgen examination at that time, and he has since been followed in this clinic with repeated roentgen and gastroscopic studies. The ulcer healed and recurred three times. On Nov. 12, 1946 roentgen examination revealed a large ulcer high on the lesser curvature of the stomach (fig. 4 *A*). On December 4 a subdiaphragmatic section of the vagus nerves to the stomach was performed. Roentgen examination twenty-one days later (fig. 4 *B*) revealed complete healing of the ulcer. This was confirmed by gastroscopy on Jan. 28, 1947 and repeated roentgen examination on January 26. Since this time, the patient has been entirely free from ulcer distress and has returned to his usual occupation. He complains occasionally of belching and postprandial distention of the upper part of the abdomen, which is completely relieved by "urecholine" (carbaminoyl-beta-methylcholine chloride).

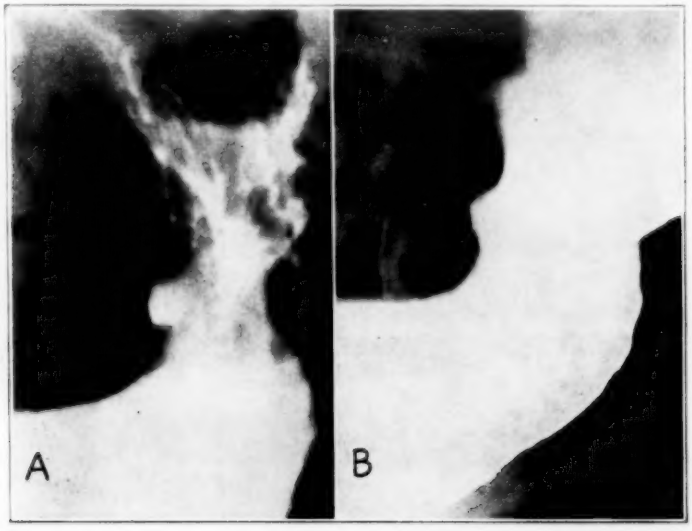

Fig. 5 (case 7).—*A*, roentgenogram showing a large ulcer crater on the lesser curvature of the stomach. *B*, roentgenogram revealing failure of ulcer in *A* to heal two months after gastric vagotomy (lesion probably malignant).

The 2 remaining patients in this series also had chronic gastric ulcers high on the lesser curvature of the stomach. In 1 patient, a diagnosis of gastric ulcer was made elsewhere two years previously, but gastrectomy was refused. The second patient had been treated for three months on the medical service of this hospital, and the ulcer had proved completely refractory to treatment. In these patients, a differential diagnosis between benign gastric ulcer and carcinoma could not

be made even with the aid of laboratory studies, roentgen examination and gastroscopic observation. Palpation and inspection of the lesion at laparotomy were also not decisive. Section of the vagus nerves to the stomach was carried out in preference to a total gastrectomy. This was done as a type of therapeutic test. Although there was complete symptomatic relief in both cases, the ulcers failed to heal, as revealed by fluoroscopic examination. Total gastrectomy was, therefore, advised.

CASE 7.—This 57 year old train dispatcher had been troubled by burning epigastric distress relieved by food since 1938. In 1942, and again in 1945, a gastric ulcer was reported to have been demonstrated by roentgen examination. He was first seen in this clinic on Feb. 11, 1946. Roentgen examination on March 4 revealed a large ulcer on the lesser curvature of the stomach. This was confirmed by gastroscopic examination. Repeated reexamination with roentgen rays and the gastroscope during the next four months revealed no evidence of healing of the ulcer on strict medical management. Roentgen examination on August 14 showed a persistent ulcer (fig. 5 *A*). The patient was admitted to the hospital for further study. The gastric content aspirated after the administration of histamine subcutaneously revealed a low concentration of free acid, and there was no free acid in the twelve hour night gastric aspiration. The patient had severe hypertensive cardiovascular disease and had suffered two previous cerebral accidents. Laparotomy was performed on August 15. A thickening of the gastric wall was palpable high on the lesser curvature posteriorly, and a sharply demarcated ulcer crater was felt in the center of this area. The lesion appeared grossly to be benign. It was decided, in view of the patient's cardiovascular disease and obesity and a rather unsatisfactory spinal anesthetic, that a total gastrectomy would be too hazardous, and accordingly a transabdominal section of the vagus nerves to the stomach was performed. The patient was promptly relieved of his ulcer distress and experienced only moderate symptoms of gastric retention. The ulcer was no longer visualized at gastroscopic examination on September 6, but on October 7 a superficial ulceration could be seen. On November 4 gastroscopic examination revealed unequivocal malignant ulceration. Roentgen examination on September 4 was unsatisfactory, but on October 8 (fig. 5 *B*) the ulcer was well visualized and, although larger and shallower, was thought to show an appearance of healing. The patient was urged to have a total gastrectomy but died of a cerebral accident at home a few days subsequently. Autopsy was not permitted. During the last few days of his life, the patient's ulcer-like distress returned to a mild degree, although his insulin reaction postoperatively remained negative.

CASE 8.—A 61 year old machinist had been bothered for sixteen years by vague, dull, epigastric pain, which had been much greater during the past two years. The relation of this distress to meals was inconstant. Roentgen examination was reported to have revealed an ulcer of the stomach two years previously, and since this time he had been on a modified medical management without much relief. Roentgen examination on admission (fig. 6 *A*) showed a large ulcer crater on the lesser curvature. This was confirmed by gastroscopy. The lesion appeared to be benign. The twelve hour night gastric aspiration revealed 240 cc. of fluid with 24 units of free acid. At laparotomy on October 23 the lesion appeared to be benign. There was a firm palpable mass with a central crater high on the lesser curvature of the stomach with adherent overlying omentum. A subdiaphragmatic section of the vagus nerves was performed with immediate relief of distress.

Roentgen examination on November 9 showed decrease in the size of the ulcer, as did roentgenograms taken on December 7 (fig. 6*B*). Roentgen examination on Jan. 7, 1947 (fig. 6*C*), however, again demonstrated the ulcer on the lesser curvature. The patient was readmitted at this time, and studies of secretion revealed no evidence of incomplete vagotomy. Total gastrectomy was advised but was refused by the patient, and he is still under observation.

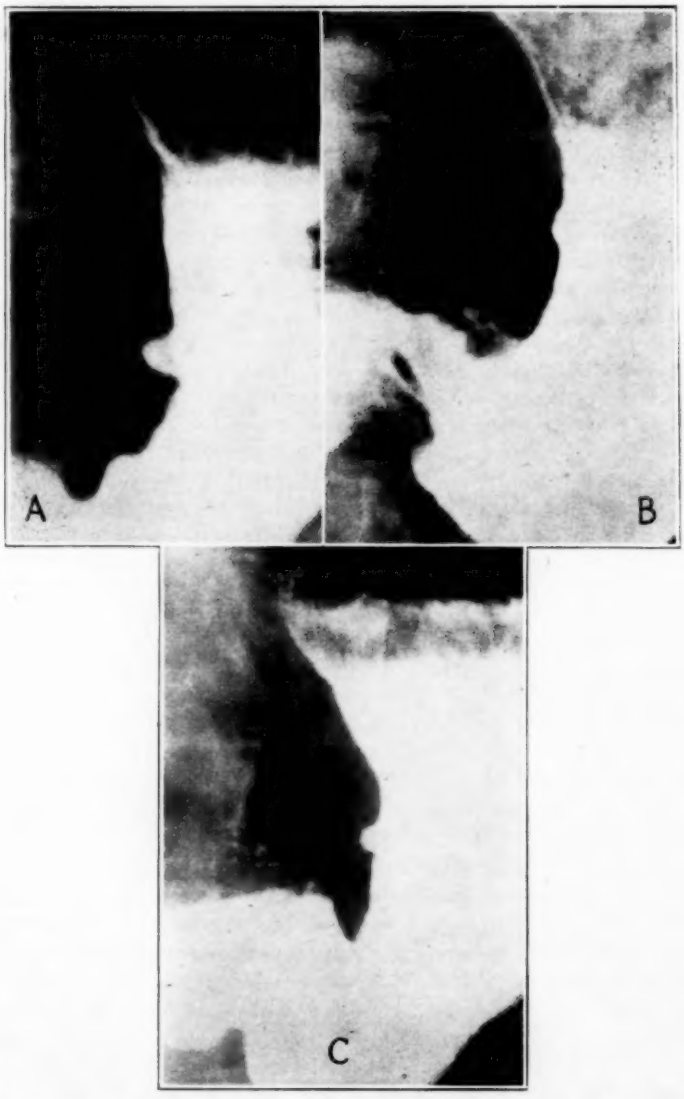

Fig. 6 (case 8).—*A*, roentgenogram showing an ulcer crater on the lesser curvature of the stomach. *B*, roentgenogram showing a decrease in the ulcer crater of *A*, six weeks after gastric vagotomy. *C*, roentgenogram showing recurrent and probably malignant ulcer, eleven weeks after gastric vagotomy.

COMMENT

In this series of patients, all the ulcers that were unquestionably benign healed promptly after the total section of the vagus nerves. The reason for this in cases with coexistent duodenal ulcer is fairly evident, as all of the patients in this category secreted large quantities of highly acid gastric juice in the empty stomach. This hypersecretion was eliminated by the vagotomy, and the ulcers healed. The patients with benign gastric ulcer alone, however, without exception displayed a low volume of night secretion with low free acidity. Although the acid secretion in these patients was reduced after the section of the vagus nerves, it is difficult to understand how such a relatively small change in the acid secretion at such a low concentration could cause prompt healing of a large ulcer in the stomach. It is likewise difficult to account for the formation of an ulcer in the gastric mucosa, which is the most resistant tissue in the body to peptic digestion, as a result of this low concentration of free acid. The possibility can be considered that a high acid secretion existed prior to the formation of the gastric ulcer and that following the formation of the ulcer, a resultant or accompanying gastritis reduced the acid secretion. There is, however, little evidence to support this hypothesis. We have, in fact, 1 patient in whom a large gastric ulcer developed in spite of a known low acid secretion for several years. The fact that gastric ulcers heal after vagotomy, although there may be only a slight change in the concentration of acid in the gastric content, suggests both that other factors than peptic digestion alone may play a role in the formation of these ulcers, and that vagotomy has some effect on these factors. What factors exist that are known to be affected by vagotomy and which could influence the resistance of the gastric mucosa to peptic digestion? The only factor in addition to secretion affected by vagotomy for which we have definite evidence is gastric motility. In addition to trauma, hypermotility might conceivably cause the removal of a protective coating of mucus from the surface of the mucosa, exposing the underlying epithelium to the action of peptic digestion. This factor might be altered by vagotomy. The possibility of other unknown and unconsidered factors is, of course, most likely. The fact remains that after total section of the vagus nerves a benign gastric ulcer usually heals and remains healed.

The treatment of gastric ulcer, however, is determined not so much by these considerations as by the fact that at the present time an accurate differential diagnosis between gastric ulcer and carcinoma cannot be made. Perhaps 20 per cent of lesions in the stomach that appear to be benign ulcers on the basis of the clinical picture and roentgen and gastroscopic examination prove to be carcinomas when studied by histologic methods. An exception to this statement must be made

for those cases with coexistent active duodenal ulcers, in which the incidence of carcinoma is considerably less than 1 per cent. Thus the presence of an active duodenal ulcer strongly suggests that the associated ulcer in the stomach is benign. We are of the opinion that these lesions can be treated satisfactorily by gastric vagotomy.

Should all other chronic ulcerating lesions in the stomach be treated by gastrectomy? The mortality following partial or subtotal gastrectomy is now less than 5 per cent. When, therefore, the lesion is in the antrum or body of the stomach and when a subtotal gastrectomy will suffice to remove it with some margin of uninvolved tissue, it seems wise to employ this procedure. Histologic examination will then determine the diagnosis, and the question of further treatment can be more intelligently considered. When, however, the lesion lies high on the lesser curvature near the esophagus, a resection to be more than a gesture would mean a total gastrectomy with possibly the removal of a portion of the lower part of the esophagus. A procedure of this magnitude carries with it an operative mortality of possibly 10 to 30 per cent and a definite digestive and nutritive disability in many of those that survive. It should not be employed unless the diagnosis of malignant growth is certain. It is in this group of gastric lesions in which vagotomy may find a field of usefulness. If the lesion is benign, section of the vagus nerves may bring about prompt healing in ulcers that have proved resistant to intensive medical management. On the other hand, if healing does not occur within a period of four to six weeks, the surgeon has additional evidence for the belief that the lesion is malignant and can undertake a total gastrectomy with a better conscience.

GASTRIC NEURECTOMY

Anatomic and Physiologic Studies with Favorable and Unfavorable Results in the Treatment of Peptic Ulcer

WALTMAN WALTERS, M.D.

HAROLD A. NEIBLING, M.D.
Fellow in Surgery

WILLIAM F. BRADLEY, M.D.
Fellow in Medicine

JOHN T. SMALL, M.D.
AND
JAMES W. WILSON, M.D.
Fellows in Surgery, Mayo Foundation
ROCHESTER, MINN.

DRAGSTEDT'S [1] report in 1946 on the section of vagus nerves in 54 cases of peptic ulcer with favorable results, similar reports by Grimson,[2] Ruffin and co-authors [3] concerning 30 cases at Duke University, and by Moore and his associates [4] concerning 12 cases at the Massachusetts General Hospital led us to study the problem of resection of vagus nerves, or, as we prefer to call the operation, "gastric neurectomy," from the anatomic, physiologic and chemical standpoint in 40

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From the Division of Surgery, Mayo Clinic (Dr. Walters) and the Mayo Foundation.

1. Dragstedt, L. R.: Section of the Vagus Nerves to the Stomach in the Treatment of Gastro-Duodenal Ulcer, Minnesota Med. **29**:597-604 (June) 1946.

2. In Grimson's most recent report (unpublished) on the results of the operation in 57 cases, he described disturbances in motility in 25. In 6 cases there was severe gastric retention which necessitated gastroenterostomy. This gave an incidence of secondary gastroenterostomy of 1 among each 7 patients who had not had a previous drainage operation.

3. Grimson, K. S.: Unpublished data. Grimson, K. S.; Taylor, H. M.; Trent, J. C.; Wilson, D. A., and Hill, H. C.: The Effect of Transthoracic Vagotomy upon the Functions of the Stomach and upon the Early Clinical Course of Patients with Peptic Ulcer, South. M. J. **39**:460-470 (June) 1946. Ruffin, J. M.; Grimson, K. S., and Smith, R. C.: The Effect of Transthoracic Vagotomy upon the Clinical Course of Patients with Peptic Ulcer, Gastroenterology **7**:599-606 (Dec.) 1946.

4. Moore, F. D.; Chapman, W. P.; Schultz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, New England J. Med. **234**:241-251 (Feb. 21) 1946.

patients operated on by one of us at the Mayo Clinic up to Jan. 15, 1947 (tables 1 and 2). Only brief reference will be made to 43 additional cases in which operation was performed by other surgeons at the clinic, for they will individually report on their results in detail later.

HISTORICAL DATA

Denervation of the stomach in the treatment of pain and peptic ulcer is not a new procedure, and an extensive and confusing literature has appeared since Brodie's [5] first report in 1814. Early and late effects of denervation of the stomach have been confused, and the results of

TABLE 1.—*Our Cases to Jan. 15, 1947*

Operation, Type	Total Cases	Operation Performed for: Duodenal Ulcer	Gastrojejunal Ulcer	Gastric Ulcer	Gastritis
Gastric neurectomy only	14	10	2	2	0
Gastric neurectomy and gastroenterostomy	15	15	0	0	0
Gastric neurectomy with excision or resection	11	3*	5	3*	1
Total	40	28*	7	5*	1

* One patient had both duodenal and gastric ulcers.

TABLE 2.—*Gastric Neurectomy: All Cases to Jan. 1, 1947*

Operation, Type	Total	Operation Performed for: Duodenal Ulcer	Gastrojejunal Ulcer	Gastric Ulcer	Gastritis
Gastric neurectomy only	32	16	14	2	0
Gastric neurectomy with gastroenterostomy	30	30	0	0	0
Gastric neurectomy with excision of ulcer	18	5*	10	3*	1
Total	80†	51	24	5*	1

* There were both duodenal and gastric ulcers in 1 case.
† Three additional patients were operated on up to Jan. 15, 1947, but were not included, at the request of the Division of Biometry and Medical Statistics.

section of the gastric and vagus nerves of man have been compared indiscriminately with those of lower animals.

Latarjet [6] after division of the gastric nerves in dogs found that (1) no grave effects followed, (2) the tonicity of the stomach was reduced, dilatation occurred and emptying time of the stomach was delayed from a normal of two to seven hours and (3) the gastric acidity was decreased, the secretion of mucus was increased and trophic lesions did not occur. He and Pauchet operated on 6 patients who had gastric

5. Brodie, B. C., cited by Hartzell.[7]

6. Latarjet, A.: Note préliminaire sur l'innervation et l'énervation de l'estomac, Lyon méd. **130**:166-167, 1921; Résection des nerfs de l'estomac: Technique opératoire; résultats cliniques, Bull. Acad. de méd., Paris **87**:681-691, 1922.

ulcers; 1 died from carcinoma later. In commenting on the results of the operation on the other 5 Latarjet stated that all had been relieved of their symptoms, had gained weight and had an increased appetite. In all 5 cases gastroenterostomy was performed at the time of the gastric denervation in the belief that it would prevent recurring ulceration in the presence of gastric stasis, for Greggion was able to produce a high incidence of gastric ulceration in rabbits by denervating their stomachs and adding to their food with a high fibrous content. The stomach of the rabbit differs from that of dog or man and, therefore, is a paunch.

In spite of this encouraging early result reported by Latarjet in 1922, a search of the subsequent French literature failed to reveal any further reports of studies or cases in which denervation of the stomach was employed.

In 1929 Hartzell [7] studied the effects of intrathoracic resection of the vagus nerves on 8 dogs. The immediate results were similar to some of those described by Latarjet; they consisted of a total abolition of psychic secretion (cephalic phase), pronounced and constant reduction of the quantity of free hydrochloric acid and of the total acids, and an increase in the p_H of the gastric secretion.

Vanzant [8] studied Hartzell's dogs and some others two and one-half years later. She found that free acid was present in all but 1 of Hartzell's original group. The effects of vagotomy on motility of the stomach were inconstant. In 4 of the dogs which she studied, emptying of the stomach was delayed; 2 had hypermotility with a tendency to diarrhea and emesis, and 3 had no change in gastric emptying time. Later results revealed the motility of the stomach of 7 of the 10 dogs she studied to be essentially normal.

ANATOMIC STUDIES

Our anatomic dissections of the gastric nerves were made on 56 men, 44 women and 11 children during the course of postmortem examinations. In ninety-two of the specimens from adults a rather regular pattern was followed in forming discrete nerve trunks from the esophageal plexus. In 8 cases, it was impossible to isolate two distinct trunks at any point, since the branches were numerous, intercommunicated and failed to follow a uniform pattern.

These anatomic studies indicated, therefore, that the gastric nerves could be located and successfully resected near the diaphragm by either a transabdominal or a transthoracic approach in approximately 92 per cent of the cases, and that possibly most, if not all, of the branches in the remaining 8 per cent also could be located in the same way.

7. Hartzell, J. B.: The Effect of Section of the Vagus Nerves on Gastric Acidity, Am. J. Physiol. **91**:161-171 (Dec.) 1929.

8. Vanzant, F. R.: The Late Restoration of Gastric Acidity After Thoracic Vagotomy in the Dog, Gastroenterology, to be published.

It is our belief that the abdominal approach is preferable to the transthoracic one for the following reasons: 1. It permits exploration of the contents of the abdomen, which may be necessary, as a Meckel diverticulum was found in 1 case and no ulcer in another. 2. It permits examination of the ulcer and its removal if it is a gastric ulcer and is suspected of being malignant. 3. It permits some type of drainage operation of the stomach if an obstructive duodenal ulcer is present or a duodenal ulcer is present that is likely to become obstructive, when gastric atony occurs after gastric neurectomy. 4. It also is useful in cases in which a gastrojejunal ulcer has followed gastroenterostomy, for in many cases repeated ulceration of the stoma has resulted in obstruction and reactivation of the duodenal ulcer. In such cases, removal of the gastrojejunal ulcer and disconnection of the gastroenteric anastomosis are necessary in addition to gastric neurectomy. 5. It permits pyloroplasty if obstruction of the duodenum has resulted from reactivation of the duodenal ulcer or from its healing after gastroenterostomy. We have tried to prevent postoperative gastric stasis and retention of secretion by anticipating that it may occur and compensating for it by a drainage operation on the stomach at the time of gastric neurectomy rather than later, and we have succeeded rather well in this purpose.

Gastric neurectomy has been performed without any other associated operative procedure in only 14 of 40 cases in which the operation has been carried out by one of us (W. W.) and in only 19 of the 43 cases in which it was performed by other surgeons at the clinic.

GASTRIC NEURECTOMY: OUR SERIES

WITHOUT OTHER GASTRIC OPERATIONS

The results in 13 of the 14 cases in which one of us performed the operation without other surgical procedures on the stomach have been satisfactory as far as measured by relief of pain, by reduction of gastric acidity and in general by reduction in gastric secretion (tables 1, 3 and 4).

Ten of these operations were performed for duodenal ulcer, two for gastric ulcer and two for gastrojejunal ulcer. One death occurred one hour after the patient had had an uneventful transabdominal gastric neurectomy. Coronary insufficiency was confirmed as the cause of death at necropsy. In this case the duodenal ulcer was producing intractable pain and the serious risk of the operation was appreciated by the surgeon and the patient. In 8 of the 10 cases of duodenal ulcer reductions in acidity occurred; in 4 of these achlorhydria developed. Eight of the patients had insulin tests; six tests revealed a flat or decreasing curve of secretion of gastric acid and two a rise in secretion of gastric acid.

Disturbances of motility with retention occurred in 4 of the cases, in 1 of which intermittent aspirations were required from the fourth

to the ninth day; in the remaining 3 considerable retention of secretion and atony of the stomach were demonstrated on roentgenologic examination.

3.—Our Cases from the Report of Nov. 1, 1946 to Jan. 15, 1947 (Included in the Total of Forty Cases)

Case	Lesion	Total and Free Acids: Before Operation	Total and Free Acids: After Operation	Minimal Blood Sugar, Mg. per 100 Cc.	Curve of Insulin Test	Roentgenologic Findings	Results
		Gastric Neurectomy with No Other Operation					
1	Perforated duodenal ulcer	80/60	28/12	26	Downward	Atony of stomach	Good relief
2	Duodenal ulcer	78/54	26/10	35	Downward	Soon after operation, duodenal ulcer present	Good relief
3	Duodenal ulcer	None	60/48	17	Upward	Retained secretion; pylorospasm	Good relief
4	Duodenal ulcer	44/36	.....	..	.....	.....	Died 1 hr. after operation, of coronary insufficiency
		Gastric Neurectomy with Simultaneous Gastroenterostomy					
5	Obstruction; duodenal ulcer	86/76	24/0	42	Downward	Nonfunctioning gastroenterostomy	Good relief
6	Obstruction; duodenal ulcer	82/72	28/16	26	Downward		
		Gastric Neurectomy with Simultaneous Gastric Resection					
7	Obstruction; duodenal ulcer	60/44	38/0	60	Flat	Atony with retention of secretion; barium remained in stoma	Early relief; fulness; no return of pain

TABLE 4.—*Free Gastric Acidity in Relation to Type of Gastric Operation in Our Cases*

Type of Operation	Total Cases	Gastric Acidity Before Operation: Determinations, Cases	Gastric Acidity Before Operation: Mean Value, Units	Gastric Acidity After Operation: Determinations, Cases	Gastric Acidity After Operation: Mean Value, Units
Gastric neurectomy only	14	10	39.4	13	9.4
Gastric neurectomy and gastroenterostomy	15	14	56.1	13	11.5
Gastric neurectomy and excision:					
Gastrojejunal ulcer	5	4	38.0	5	18.8
Gastric ulcer	3	3	20.0	3	0
Duodenal ulcer	2	2	46.0	2	0
Gastritis	1	1	42.0	1	0
Total	11	10	33.1	11	9.4
Grand total	40	34	40.3	37	10.1

In the 2 cases in which small gastric ulcers were present achlorhydria developed after the operation. Insulin tests gave negative results. In 1 of these patients atony of the stomach developed which continued

for at least eight weeks. Although this patient was relieved of pain after his operation, he complained of discomfort and a feeling of fulness in his stomach when he had eaten a small amount of food at mealtime. At the time of reexamination at the clinic the stomach was so dilated and there was so much secretion that the roentgenologist was unable to determine whether the gastric ulcer had healed or not. Unfortunately gastroscopic examination was not made, but one will be at the patient's next visit.

WITH OTHER GASTRIC OPERATIONS

Duodenal Ulcer.—In 15 cases in which duodenal ulcers were present gastroenterostomy (table 1) was performed simultaneously with gastric neurectomy. In 7 of this group relative achlorhydria developed; in 4 reduction of gastric acidity was marked, and in 1 no reduction occurred. In 1 of the remaining 3 no preoperative studies of gastric acidity were performed, but postoperative studies revealed total acidity of 34 and free acid of 22 (Töpfer's method). In 2 cases no postoperative studies of gastric acidity were carried out.

Troublesome disturbances of gastric motility developed in 4 of these cases. In 1, the retention continued for twenty-six days, and a jejunojejunostomy was necessary. However, the gastroenterostomy in this case was an anterior one.

One patient had such a degree of abdominal distention from the fifth to the seventh day after operation that an intestinal obstruction was thought likely, and roentgenologic examination indicated that it was present. Abdominal exploration revealed that the entire gastrointestinal tract was filled with fluid and gas, and 800 cc. of sterile straw-colored fluid was present in the abdominal cavity. The patient's gastrointestinal motility returned to within normal limits in a few days after continuous aspiration of the gastrointestinal secretions by an indwelling Wangensteen suction tube.

Another patient had retention daily. Occasionally a maximum of 2,000 cc. was found. The quantity of retained secretions decreased gradually until the fourteenth day after operation. Six months later the patient reported by letter that he had a recurrence of his symptoms of ulcer with vomiting.

Gastric Ulcer.—Three patients had large gastric ulcers. All were high on the posterior wall of the stomach and had perforated onto the pancreas. Partial gastrectomy for removal of the ulcers would have necessitated removal of most of the stomach. It seemed best, therefore, to excise the ulcers and to see what the effects of gastric neurectomy would be. In 1 of these cases a recurring gastric ulcer developed with severe ulcer symptoms, including bleeding and associated anemia. In the second case complete relief from pain occurred after operation while

an unrestricted diet was being given, but the patient complained of frequent belching of foul gas for four months. Roentgenologic examination gave evidence of a dilated stomach with spasm in the prepyloric area and hypomotility of the small intestine. There was so much secretion at the end of a five hour period that the roentgenologist could not tell whether gastric ulcer had returned or not. Gastroscopic examination revealed no recurrence of his gastric ulcer.

Gastrojejunal Ulcer.—Five patients were treated for gastrojejunal ulcers by gastric neurectomy and additional procedures (table 1).

In 1 of these cases the ulcer had occurred after partial gastrectomy was done elsewhere. Its large crater was on the transverse colon. It seemed advisable in this case to resect the stomach to remove the ulcer, and to perform a gastric neurectomy rather than to do the latter procedure alone because of the uncertainty of whether the ulcer would heal and of whether it would produce obstruction at the stoma. Achlorhydria developed after operation. Unfortunately an insulin test was not done in this case. No clinical retention was noted and roentgenologic examination revealed normal motility. There was good relief of symptoms.

Two patients had gastrojejunal ulcers of considerable size with deformities of the gastroenteric stoma and deformities of the duodenum as a result of the healing of their duodenal ulcers. After the gastroenteric anastomosis was disconnected, the gastrojejunal ulcer was removed in each case and pyloroplasty was performed for the relief of the duodenal obstruction. Achlorhydria did not develop in either of these cases in spite of negative reactions to the insulin tests. It will be interesting to see what the future course of these 2 patients will be, for experience has shown that there is a 60 per cent recurrence of the duodenal ulcer in cases in which the procedure just described has been performed without associated gastric neurectomy. In 1 of these 2 cases gastric retention of secretion occurred from the fourth to the sixth day. In 1 of these cases pylorospasm was noted on roentgenologic examination; in the other, a slightly atonic stomach was found.

In the remaining 2 cases the gastroenteric anastomosis and the gastrojejunal ulcers were removed and reconstruction of the stomach and jejunum was carried out. In 1 of these 2 cases achlorhydria developed. In the other case a total gastric acidity of 20 units and free hydrochloric acid of 6 units were observed after operation but no preoperative studies of gastric acid were made. Insulin tests in both cases were negative in result. Neither had disturbances of motility.

In the cases of gastrojejunal ulcer, the immediate results of the operation have been satisfactory.

GASTRIC NEURECTOMY: OTHER CLINIC SURGEONS' SERIES

WITHOUT OTHER GASTRIC OPERATIONS

Gastric neurectomy without other surgical procedures has been performed in 19 cases by other surgeons at the clinic. In 14 cases the operation was done transthoracically and in 5 transabdominally.

Transthoracic Approach: Five patients who had duodenal ulcers and 9 who had gastrojejunal ulcers were operated on transthoracically. Eleven had preoperative and postoperative studies of gastric acids. In 5 of the cases of gastrojejunal ulcer and in 1 of duodenal ulcer achlorhydria developed. In 2 cases of duodenal ulcer and in 1 of gastrojejunal ulcer no reduction of acidity occurred. Postoperative roentgenologic studies were made in 8 cases. In 2 of the cases of gastrojejunal ulcer evidence of jejunitis continued. In one case achlorhydria developed, but no reduction of acid occurred in the other. Four patients had delayed emptying of the stomach. In 1 patient it was so prolonged (two months) that anterior gastroenterostomy was performed. This case will be referred to later.[9] In another, pain from a duodenal ulcer with night pain which required foods and alkali for relief has continued.

Two patients had troublesome diarrhea after operation; one of these had a return of symptoms of ulcer and the other had nausea and vomiting in addition. One patient died after a convulsion on his fourth postoperative day.[9]

Transabdominal Approach: Two patients who had duodenal ulcers and 3 who had gastrojejunal ulcers underwent transabdominal gastric neurectomy. Only 1 of these patients had complete relief of symptoms. One of the patients who had a duodenal ulcer had symptoms of bloating, belching and vomiting four months after operation, and, although he had no ulcer pain, a roentgenogram showed a persisting duodenal ulcer.[9] One of the patients who had a gastrojejunal ulcer had persistent symptoms of ulcer with disturbances of gastric motility which required aspiration for one month after operation. Roentgenologic examination revealed evidence of a poorly functioning gastroenteric stoma with distortion of the jejunum, and the presence of a gastrojejunal ulcer could not be ruled out.[9]

WITH OTHER GASTRIC OPERATIONS

In 24 cases additional gastric operations were performed simultaneously, in 19 for duodenal ulcer and in 5 for gastrojejunal ulcer.

Duodenal Ulcer.—Sixteen of the patients who had duodenal ulcer had associated gastroenterostomy and 3 had pyloroplasty. In 11 of the group who underwent gastroenterostomy preoperative and postoperative studies of gastric acidity were carried out. Nine patients had

9. This case will be referred to again in the section on "Recurrence of Ulcer or Failure of Ulcer to Heal: Both Series."

marked reduction of gastric acidity, and 4 of these had achlorhydria. Two had no reduction of acidity. Temporary moderate disturbances of motility were noted in 5. One of the patients had a perforating duodenal ulcer and died on the fourteenth postoperative day.[10]

In all of the 3 cases in which pyloroplasty was performed gastric acidity was reduced considerably after operation from a high preoperative level, but in one of these cases clinical evidence of disturbance of

TABLE 5.—*Failure of Ulcer to Heal After Gastric Neurectomy*

Case	Lesion	Gastric Neurectomy	Other Operation	Gastric Acids		Roentgenologic Observations	Results
				Before Operation	After Operation		
8	Gastric ulcer and duodenal ulcer	Transthoracic	Excision through diaphragm	64/52	40/26	Persistent gastric ulcer	Resection of stomach *
9	Duodenal ulcer	Abdominal	None	74/56	40/20	Duodenal ulcer 3 mo. after operation	Fulness; bloating; vomiting; no pain; some diarrhea
10	Duodenal ulcer	Transthoracic	None	70/56	56/30	Retention with obstruction at pylorus	Retention; gastroenterostomy 2 mo. after operation; troublesome retention 1 mo. after gastroenterostomy
11	Gastrojejunal ulcer	Transthoracic (elsewhere)	None	.....	40/28	Dilated jejunal loops; gastrojejunitis	Several hemorrhages; resection of stomach; large gastrojejunal ulcer
12	Gastrojejunal ulcer, jejunitis	Transthoracic	None	100/80	60/48	Poor function; gastrojejunal ulcer could not be ruled out	Return of pain 2 mo. after operation; diarrhea
13	Gastrojejunal ulcer	Transthoracic	None	40/20	12/0	Gastrojejunitis	Diarrhea and nausea
14	Gastritis	Abdominal exploratory	Exploratory gastrostomy	54/42	80/0	Atony of stomach; gastritis; gastric ulcer (?) on lesser curvature *	Symptomatic relief *

* Insulin test was negative in result.

gastric motility was present and in another pain was occurring at night at the time of dismissal.

Gastrojejunal Ulcer.—Resection of the stomach was performed in 1 case of bleeding gastrojejunal ulcer. Transthoracic resection of the vagus nerves had been performed elsewhere six and one-half months previously, without benefit to the ulcer.[10] Excision of the gastrojejunal ulcer and disconnection of the gastroenteric anastomosis were per-

10. This case will be referred to again in the section on "Recurrence of Ulcer or Failure of Ulcer to Heal: Both Series."

formed in 3 cases, in 2 of which pyloroplasty was performed also. One patient, who died at home three months after operation from a coronary occlusion, had a fistulous opening into the colon closed.

RECURRENCE OF ULCER OR FAILURE OF ULCER TO HEAL: BOTH SERIES

One of the patients operated on by one of us (W. W.) had a recurring gastric ulcer (table 5). This patient, a Jew 67 years of age, had had a gastrojejunal ulcer which had been removed at a previous operation when the gastroenteric stoma was closed. Subsequent to the operation, achlorhydria developed. The insulin test (table 6) gave negative results, and disturbances of gastric motility were not pronounced, although slight retention was noted soon after gastric neurectomy. Roentgenologic examination on Oct. 17, 1946 disclosed a return of the gastric ulcer with an atonic stomach. This resulted in spite of a careful and well controlled medical regimen which was continued for

TABLE 6.—*Results of Insulin Test in a Case of Recurring Gastric Ulcer*

		Time After Injection of Insulin, Min.			
	Fasting	15	30	45	60
Sept. 18, 1946:					
Blood sugar, mg./100 cc.	103	89	68	48	45
Total acid, units	26	12	12	10	10
Free hydrochloric acid, units	10	0	0	0	0
Amount of gastric secretion, cc.	30	10	15	35	40
Jan. 7, 1947:					
Blood sugar, mg./100 cc.	105	113	72	47	35
Total acid, units	26	8	10	10	0
Free hydrochloric acid, units	10	0	0	0	0
Amount of gastric secretion, cc.	45	8	10	20	60

five and one-half months. In January 1947 the patient complained of pain in the region of the left supraspinatus muscle and down his left arm. This pain was thought to be due to extension of the inflammation from the ulcer to the diaphragmatic portion of the peritoneum. The results of insulin test (table 6) were essentially the same as at the time of the previous examination except that the curve was even flatter. A histamine test resulted in a marked elevation in acids. On January 13 Dr. Waugh performed a Hofmeister-Polya resection of the stomach; a benign gastric ulcer with a crater 3.5 cm. in diameter was removed with the resected portion of the stomach.

Two cases (table 5) in which our colleague, Dr. Priestley, performed the operations are worthy of mention. In 1 of these cases (case 11, table 5) transthoracic gastric neurectomy had been performed elsewhere for gastrojejunal ulcer; hemorrhage from the ulcer had occurred ten hours after the operation and again several weeks later. When the anastomosis was taken down and the patient's stomach was resected, an active gastrojejunal ulcer with a crater and pronounced

jejunitis was found. In the second case (case 10) Dr. Priestley felt it necessary to perform a drainage operation on the stomach twelve days after transthoracic gastric neurectomy because of failure of the stomach to empty properly. As much as 500 cc. of gastric secretion was removed at one time in this case before the second operation. An active duodenal ulcer was found at operation and the pylorus was patent. Anterior gastroenterostomy was performed, but retention of gastric secretion in larger amounts began on the twelfth day following operation and continued for more than thirty days. Unfortunately it was not possible to perform the Hollander insulin test in either of these cases to determine whether all branches of the vagus nerves were divided.

In a recent report by Colp[11] of 33 cases of ulcer treated by supradiaphragmatic resection of the vagus nerves, gastric resections were required in 4 from two to seven months later. Disturbances in motility made resection necessary in 3 and persistent symptoms of ulcer in the other case. Of the 33 patients, he considered only 18 as well. One patient had recurring hemorrhages thirteen months after operation, and 1 died from hemorrhage into the left adrenal gland fourteen days after operation.

In another case of duodenal ulcer in which transabdominal gastric neurectomy was performed by one of our colleagues, relief of pain was obtained but bloating, belching and vomiting continued for four months after operation and roentgenograms indicated a persisting duodenal ulcer.

One of the patients who had a transabdominal gastric neurectomy for a gastrojejunal ulcer had persistent symptoms of ulcer with disturbances of gastric motility which required aspiration for one month after operation. Roentgenoscopic examination disclosed a nonfunctioning gastroenteric stoma with distortion of the jejunum. A gastrojejunal ulcer could not be ruled out.

Schiff[12] has told us of 1 of his patients who had duodenal ulcer, which failed to heal after resection of the vagus nerves. Subsequent partial gastrectomy was made necessary because of a continuation of symptoms of ulcer and hemorrhages. The presence of an ulcer was proved at the time of operation.

DEATHS FOLLOWING GASTRIC NEURECTOMY

In addition to the death from coronary insufficiency which occurred in 1 of our cases, death occurred in 3 other cases in the 83 under consideration. It occurred on the fourteenth postoperative day in 1 case in which gastric neurectomy and gastroenterostomy were performed. Gastric retention and hypoproteinemia were the only significant post-

11. Colp, R.: Unpublished data.
12. Schiff, L.: Personal communication to the authors.

operative symptoms in this case. Postmortem examination revealed an unsuspected perforation of the duodenal ulcer and subdiaphragmatic abscess. In another case, in which gastric neurectomy, cholecystectomy and appendectomy were performed, the patient died after a convulsion on the fourth postoperative day. Unfortunately consent for postmortem examination could not be obtained. Another death from coronary disease was reported to us by the patient's physician in his home locality. It occurred three months after gastric neurectomy for gastrojejunocolic fistula in which the fistula into the colon was closed at the time of operation.

Recently Weeks and his associates,[13] working at Bellevue Hospital, reported 2 deaths following transthoracic resection of the vagus nerves. One of these deaths was due to an unsuspected perforation of the duodenal ulcer seven weeks after operation, and the other death occurred on the operating table when traction was being placed on the left vagus nerve. In the former case, resection of the left splanchnic nerve had been done at the time of the transthoracic resection of the vagus nerves and that of the right splanchnic nerve a week previous to the perforation of the ulcer. In the second case the death was of a cardiac type, but no necropsy was done.

COMMENT AND SUMMARY

Our studies on gastric neurectomy indicate that the results are inconstant, variable and in most cases unpredictable. The relief of pain obtained may be the result of the release of gastrospasm and a reduction in gastric acidity as a result of the interruption of cephalic stimulation. The expense of this relief of pain is dilatation of the stomach with frequent troublesome retention of gastric secretion and in some cases remnants of food. Moreover, that relief of pain is not the result of healing of the ulcer must be considered, since in 1 of our cases unsuspected acute perforation of duodenal ulcer developed. A similar case has been reported by Weeks and his associates.[13]

In 1 case a gastric ulcer recurred; in other cases failure of the ulcers to heal has been demonstrated pathologically at subsequent operations necessitated by a continuation of bleeding or a marked degree of gastric retention which interfered with the patient's nutritional state.

Reduction in gastric acidity, although it has occurred in most cases, is inconstant in others, and the disturbances of motility of the stomach and small intestine are frequent after operation. In some cases these disturbances are temporary, and in others are prolonged, persistent and troublesome to the patient. In such cases, patients have complained of frequent belching of foul-smelling gas and fulness and bloating after

13. Weeks, C.; Ryan, B. J., and Van Hoy, J. M.: Two Deaths Associated with Supradiaphragmatic Vagotomy, J. A. M. A. **132**:988-990 (Dec. 21) 1946.

meals, and a few have complained of nausea and diarrhea. As has just been mentioned, subsequent operations have been necessary in some cases to remove the persistent ulcer or to provide drainage.

There have been 3 hospital deaths in the 83 cases. Although 2 of these could be directly attributed to cardiovascular accidents, 1 patient died of unsuspected perforated duodenal ulcer with a subdiaphragmatic abscess. Gastroenterostomy had been done at the time of the gastric neurectomy. Another patient died from a coronary occlusion at home three months after the closure of a gastrojejunal colic fistula.

In evaluation of the results of the operation it must be proved that an ulcer is present and that the gastric nerves have been completely sectioned. It is our opinion that the best approach in most cases in which gastric neurectomy is contemplated is by means of a transabdominal incision, for this approach permits exploration of the gastrointestinal tract and such procedures as are necessary to supplement the gastric neurectomy. The greatest field of usefulness for the operation seems to be in the treatment of ulcers after partial gastrectomy and in certain cases of nonobstructive duodenal ulcers in which the cephalic phase of gastric secretion is marked and pain is intractable.

In view of the inherent ability of the gastrointestinal tracts of human beings, like those of animals, to regain through compensatory mechanisms their function after operative procedures which disturb the neuromuscular continuity, and in view of the fact that restoration of gastric acidity and gastric motility has occurred within two years in dogs in which gastric neurectomy has been performed, the possibility of such a return in human beings must be kept in mind.

For the time being the operation of gastric neurectomy will have to be considered as in the investigative stage.

NOTE.—Since this paper was written 1 patient has died at home eight months after operation from gangrene of the terminal part of the ileum. This patient is the one who had abdominal distention from the fifth to the seventh day after gastroenterostomy and gastric neurectomy, at which time abdominal exploration was performed but no obstruction was found. The gastrointestinal motility then returned to normal after continuous gastric aspiration.

Another patient, the one who had retention for twenty-six days after anterior gastroenterostomy and gastric neurectomy and then underwent jejunojejunostomy, now has a gastrojejunal ulcer. His negative insulin reaction (Aug. 5, 1947) showed that all branches of the vagi to the stomach had been resected.

RESECTION OF THE VAGUS NERVES FOR ULCER: AN INTERIM EVALUATION

I. Operative Technic and Hospital Management

FRANCIS D. MOORE, M.D.
Assistant Professor of Surgery, Harvard Medical School; Assistant Surgeon, Massachusetts General Hospital
BOSTON

RESECTION of the vagus nerves for ulcer, like any other application of autonomic surgery, may be considered to embody three rather distinct areas for study and development. The first of these concerns the technical procedure itself, its extent, its intrinsic surgical complications and the immediate hospital morbidity and mortality. The second area embodies the physiologic response of the patient. No autonomic nerve can be interrupted, be it the presacral plexus, the lumbar sympathetic, the splanchnic nerve, or the vagus, without producing physiologic changes, an understanding of which is absolutely essential to intelligent clinical application of the procedure. The third area in this field involves close examination of the clinical end results. Clinical results may be extremely variable in their degree of dependence on the first two factors.

In this paper it is my wish to outline the technical procedures which my colleagues and I have employed in vagus resection for ulcer as well as the hospital management of patients. We previously described the physiologic effects of the operation.[1]

The clinical results in the patients operated on to date will be described in the subsequent paper.[2] The study of resection of the vagus nerves at the Massachusetts General Hospital comprises at the present time a group of 84 patients who have had this operation performed. There are 4 patients in this group who have had resection of the vagus nerves for diseases other than peptic ulcer. Six patients have been operated on too

Read at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 22, 1947.

1. Moore, F. D.; Chapman, W. P.; Schulz, M.D., and Jones, C. M.: (*a*) Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, New England J. Med. **234**:241-251 (Feb. 21) 1946; (*b*) Resection of the Vagus Nerves in Peptic Ulcer: Physiologic Effects and Clinical Results, with a Report of Two Years' Experience, J. A. M. A. **133**:741-748 (March 15) 1947.

2. Moore, F. D.: Vagus Resection for Ulcer: An Interim Evaluation; II. Clinical Results, Ann Surg., to be published.

recently to be of value in any consideration of clinical effects. The remaining 74 patients will form the subject of this discussion.

I. SURGICAL TECHNIC

1. *Essential Conditions.*—The operative technic used in this study has been developed to include the following essential features:

(*a*) A thorough dissection should be done with adequate exposure under satisfactory conditions of lighting and availability of the field. These conditions are best satisfied by a thoracic approach.

(*b*) The only way that we know of definitely establishing the fact that all of the fibers of the trunks of both vagus nerves have been sectioned is to follow the nerves downward to their point of decussation on the stomach wall.

(*c*) The gastrointestinal tract is allowed to retain its normal continuity, providing that previous surgical treatment has not been given. No gastroenterostomy is carried out at the time of resection of the vagus nerves or afterward unless clinical necessity demands it—a rarity in our experience. The importance of this seems self evident. Placing jejunal mucous membrane in the stomach has been a source of difficulty since the introduction of posterior gastroenterostomy as a treatment for ulcer many years ago. Jejunal mucosa is much more vulnerable to gastric secretion than duodenal. In addition, posterior gastroenterostomy alone will confer satisfactory results on the healing of ulcers in a certain fraction of cases. If one concedes that resection of the vagus nerves is also a useful operation, it is then clear that the performance of a posterior gastrojejunostomy with resection of the vagus nerves will confuse the interpretation of the clinical results.[2a]

(*d*) Steps to prevent regeneration should be taken. This is accomplished by resection of a portion of the nerves and enclosure of the proximal ends in some sort of an impermeable sheath.

2. *Preparation for Surgery.*—So far as patients who are acutely bleeding or who have frank obstruction have not beeen routinely subjected to resection of the vagus nerves, these physiologic problems have not presented themselves in the preoperative preparation. However, a number of patients have been operated on who had recently been bleeding either from a duodenal or a jejunal ulcer. It has been our policy in such cases to permit the bleeding to subside completely and to institute a seven to ten day period of intensive medical therapy before proceeding with surgical treatment. This has usually been effective, as it is one of

2a. In addition, it has become apparent that performance of a gastroenterostomy suffices but little to lower the incidence of motility disorders except in the presence of advanced obstruction, in which case its performance will abate the obstruction, but other motor side-effects will persist with their incidence unchanged.

the characteristics of bleeding ulcers, especially painless bleeding ulcers, to heal rapidly once the bleeding has ceased. Two experiences which we have had with patients who have bled massively from the gastrointestinal tract within a week of vagus resection have led us to believe that in patients who have been bleeding recently, resection of the vagus nerves should be employed after the ulcer has been given a period of medical management.

In the case of painful, intractable ulcer without obstruction most characteristic of this group, attention is directed to the patient's general status relative to anemia, hypoproteinemia, malnutrition, renal stones, alkalosis or chronic disease of the lungs. In most cases an overnight secretion test by multiple sampling followed by an insulin test is carried out to provide a base line for future study. We have not found these tests to be of value in the selection of patients or in the prediction of results; they are omitted if the patient's clinical condition (i. e., severe pain on fasting) contraindicates them.

Either just before or just after the induction of anesthesia, a Levin tube is inserted into the stomach. This is useful in the mobilization of the esophagus and is also used postoperatively.

3. *Anesthesia and Operative Technic.*—Anesthesia by intratracheal administration of gas-oxygen-ether has been used in all the patients who have had this operation. It produces conditions satisfactory for the surgeon and has been followed by a remarkably low incidence of pulmonary complications.

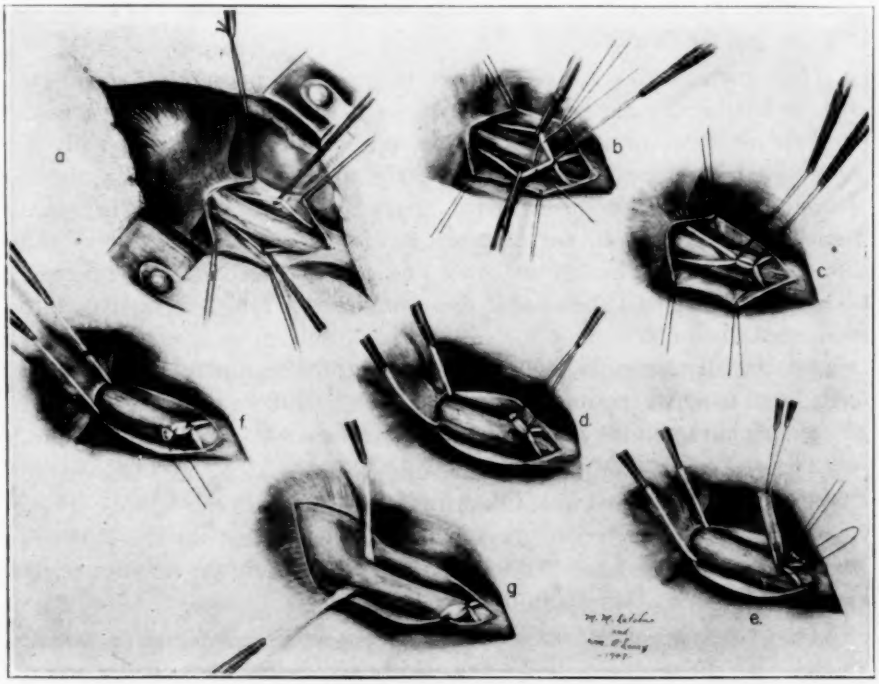
The chest is opened through the bed of the eighth, ninth or tenth rib, depending on the conformation of the patient. It is helpful to consult a roentgenogram of the patient's chest and to select the rib which in midaxilla is opposite the dome of the diaphragm.

After the chest has been opened, the mediastinum is entered by severing the inferior pulmonary ligament. Care should be taken to preserve the mediastinal reflection of the parietal pleura, as it greatly facilitates closing the mediastinum. In our early cases the esophagus was freed throughout its entire circumference and placed on traction during dissection of the nerves. We have since found that this is unnecessary and that a much more facile dissection can be carried out if the esophagus is allowed to drop back into the mediastinum as soon as the nerve trunks are picked up. In this fashion it is necessary to interrupt less of the esophageal blood supply.

There is considerable variability in the anatomic arrangement of the major branches of the vagus nerves. In the minor details of branching and arborization there is even greater variability. The important single anatomic fact remains that there are two vagus nerves running down along the esophagus to the stomach in the vast majority of patients. When the diaphragm is opened in a large series of cases, the truth of this

assertion becomes increasingly evident. One finds that there are two arborizations of the vagus nerves on the stomach wall, not more than two and not less than two. Above this area (in and immediately above the diaphragm) there are variable arborizations and anastomotic branches running between the two nerves, but the constancy of decussation on the stomach wall in itself provides adequate justification for dissecting the nerves down to their point of decussation. It is by this maneuver only that one can be assured of sectioning all the nerve fibers.

Two recent studies have clarified some of the anatomic problems involved, though the authors have come to quite different conclusions



Diagrammatic sketch of operative technic employed in thoracic vagus resection. No effort is made to portray in detail the variable anastomotic branches of the vagus nerves above the diaphragm. (*a*) The chest having been opened through the bed of the ninth rib, the mediastinum is opened, and the two nerves identified. (*b*) and (*c*) The two nerves are sutured together at two points 2 cm. apart. (*d*) The nerves are severed below the distal suture. (*e*) The proximal end of a silk cylinder is sutured to the proximal suture on the nerve trunks. (*f*) the silk cylinder is divided and ligated distal to the cut ends of the enclosed nerves. (*g*) The silk cylinder is sutured on or into the pleura so that there is no tension in the nerves. The diaphragm is opened (this step can be dispensed with if a slack hiatus permits delivery of the upper part of the stomach into the chest). The nerves are dissected downward to the point where they broaden out and divide into multiple fibers for decussation into the subserous layers of the stomach. They are divided at that point; diaphragm, mediastinum and chest are closed with interrupted silk sutures.

from their dissections. Walters and his group [2b] studied 100 adult subjects and found that 64 had well formed, common vagus trunks; 7 had extensive plexuses, but these nerves joined as well defined trunks before decussating on the stomach; 21 had long discrete trunks, characterized by few intercommunications, and the remaining 8 had atypical branches which left the trunks in the thorax. Despite the authors' conclusion that 10 per cent of the dissections disclosed patterns which were "not uniform" in the thorax, they concluded that the subdiaphragmatic approach is satisfactory. Miller and Davis [3] dissected 13 cadavers, found essentially the same conditions, and concluded that a supradiaphragmatic operation is preferable. This conclusion would seem well warranted by the findings of atypical branches in about 10 per cent of the cases in the thorax.

This anatomic point is emphasized because no amount of dissection in the mediastinum can replace the downward tracing of the nerve trunks to their major arborization on the stomach wall as a means of positively identifying and removing the total nerve mass. Likewise, no subdiaphragmatic dissection will reveal the atypical mediastinal branches which occur in 8 to 10 per cent of cases, as described by Walters and his co-workers.[4] Though one may find variable mediastinal branches, downward dissection shows that these branches arrange themselves into two trunks prior to decussation in the gastric subserous layers. For this reason the diaphragm has been opened in the majority of cases; in occasional patients the diaphragmatic hiatus is sufficiently patent so that the gastric decussation can be identified without incising the diaphragm.

The two nerves are sectioned about 3 inches (7.6 cm.) above the diaphragm and enclosed in a silk cylinder, as shown in the figure. They are dissected downward to their point of arborization on the stomach wall, where they are again sectioned at the point where the nerve spreads out to divide into filaments in the seromuscular coat.

The circumference of the esophagus is checked for small fibers which plunge into the muscular walls and which may be divided at this point.

2b. Bradley, W. F.; Small, J. T.; Wilson, J. W., and Walters, W.: Anatomic Considerations of Gastric Neurectomy, J. A. M. A. **133**:459-461 (Feb. 15) 1947.

3. Miller, E. M., and Davis, C. B., Jr.: An Anatomic Study of the Vagus Nerves, J. A. M. A. **133**:461-462 (Feb. 15) 1947.

4. We have not routinely employed any of the available cholingeric drugs (Machella, T. E.; Hodges, H. R., and Lorber, S. N.: The Restoration of Gastric Motility by Urethane of B-Methyl Choline After Section of the Vagus Nerves for Peptic Ulcer, Gastroenterology **8**: 36-51 [Jan.] 1947) in the postoperative period. Their routine use might lower postoperative difficulties. Such drugs might also produce enough acid and motor reaction so as to delay both healing and the postoperative local "take-over" of the denervated stomach which, at the fourth to sixth month, is usually correlated with the disappearance of side-effects.

Their importance is difficult to assess, but it has been our practice to "clean" the esophagus through the area of dissection.

The diaphragm is then closed, leaving a hiatus that is snug but not tight; the mediastinal pleura is partially closed, and the chest is closed in layers without drainage. It has been our practice to aspirate the small quantity of occluded air from the chest with a catheter as the chest is closed. We have not used drainage in these cases and have had to resort to thoracentesis in only 3 cases.

Approximately 85 per cent of the patients in this series have been operated on by this method. One patient had an abdominal vagotomy with simultaneous posterior gastroenterostomy; 1 patient with pyloric obstruction had a preliminary posterior gastroenterostomy followed at a second stage by thoracic resection of the vagus nerves, both patients being treated in this fashion for purposes of special study. A few patients have had a supradiaphragmatic resection with no effort made to trace the nerves downward to their point of decussation.

II. POSTOPERATIVE MANAGEMENT

The postoperative handling of these patients may be divided into three categories: the management of the chest, of the stomach and of the patient's over-all clinical and nutritional condition.

The prevention of pulmonary complications involves early ambulation, the use of blow bottles, encouraging the patient to cough and take deep breaths and moving the patient freely in the bed. A firm, but not tight, thoracic binder gives the patient some sense of support and may help him in coughing and deep breathing. If the temperature is not returning to normal by the third day, a roentgenogram is taken, and if any significant amount of collapse persists bronchoscopy may be performed.

The postoperative management of the stomach is, of course, of the greatest importance. It is our impression that the early postoperative course of these patients, and possibly the late postoperative course, are more profoundly affected by the details of postoperative management of the stomach than by any other single factor. The dietary regimen should be essentially similar to that following a subtotal gastrectomy. The patient should be given only small amounts of fluid (less than 1 ounce [30.0 cc.] an hour) for three to four days. The diet should then be started up cautiously; the stomach should be aspirated daily, and the diet should be "set back" if significant residue forms. Small amounts of solid food are far preferable to liquids.

It has been our practice to leave the Levine tube in place on suction for forty-eight hours in most cases. In occasional patients who have symptoms referable to the respiratory tract or a sensitive naso-

pharyngeal mucosa we have removed it earlier than this. In 1 patient with advanced bronchiectasis, in whom the tube was removed early in the hope of improving bronchial evacuation by cough, acute dilatation of the stomach occurred and doubtless would have been prevented had the tube been left in longer. This was the only frank acute dilatation of the stomach that we have had.

The patient should never be discharged from the hospital prior to the twelfth day. In several instances in which patients were discharged prior to the twelfth day they returned with troublesome symptoms which doubtless could have been prevented by longer hospitalization and more gradual dietary increase.

If the patient is kept in the hospital from twelve to fourteen days he becomes more familiar with his dietary limitations and has a smoother postoperative course. It should be emphasized that diarrhea in these patients is definitely associated with gastric distention and that the prevention of the latter is an important feature in controlling diarrhea. It, therefore, becomes evident that controlling the diarrhea is, in part, a problem in control of the patient's diet.

At the time the patient is discharged, he is given a sheet of instructions which include directions which he should follow in case of difficulty with diarrhea or fulness. The use of hot strong tea three times a day with or without the addition of camphorated tincture of opium is a useful adjunct in the treatment of diarrhea. It has been much more effective than some of the more complicated pharmacologic preparations. If the patient has "bouts" of fulness—which may often be accompanied by diarrhea—he is advised to stop eating completely for twelve hours and then to start eating small amounts of solid food. It has been a common experience in these patients that solid foods are tolerated better than liquid food. This seems at first glance to be a contradiction. On the other hand, one is not dealing with cicatrical pyloric stenosis in most of these cases, and when the pylorus opens it opens to a satisfactory extent. The difficulty is simply that the peristaltic action of the stomach is ineffectual in propelling the material through the pylorus. It is apparently the case that gastric peristalsis handles a bolus of solid food better than liquid after resection of the vagus nerves. Patients have stated repeatedly that small amounts of solid feeding are better tolerated by them than liquids. Liquids give them the "full" feeling, while solids do not. This fact may account for the peculiar contradiction often noticed that patients are nutritionally well and not complaining of symptoms despite large amounts of barium residual on a test meal. The use of solid foods after the fourth postoperative day has been found helpful in the early postoperative period, possibly for these same reasons.[4]

III. HOSPITAL MORBIDITY AND MORTALITY

The hospital morbidity from this operation may be considered as falling into two categories: (1) prolonged hospitalization due to difficulty in gastric emptying or other factors related to the gastrointestinal tract and (2) those postoperative complications including atelectasis, fluid, or other disorders of the chest directly attributable to the operation.

In general, the importance of both these complications together may be judged by the length of the hospital stay. If complications pertaining either to the chest or to the stomach occurred which did not prolong the patient's stay beyond fourteen days, they cannot be adjudged a major difficulty. If, on the other hand, the patient's stay in the hospital was unduly prolonged due to factors arising from either cause, such factors must then be considered to be a major complication.

In the 74 cases under consideration, 11 patients had to stay in the hospital longer than fourteen days. Only 3 of these patients remained in the hospital twenty days or longer, and the longest stay was twenty-nine days. One patient, originally discharged from the hospital on the twelfth day, had to be readmitted within a week because of disorders of emptying which passed off with further hospital supervision.

Examination of the records of the patients who remained in the hospital more than fourteen days indicates that approximately two thirds of them were slow in being discharged because of time required to get them stabilized on a satisfactory diet. Only a few remained because of difficulties attributable to the chest. There is 1 patient in whom multiple chest taps had to be carried out because of collection of serosanguineous fluid the origin of which was undoubtedly traceable to poor hemostasis at operation. One patient had a phlebothrombosis requiring ligation of a vein. A bleeding episode fourteen days after operation (discussed in a later paragraph) necessitated a hospital stay longer than usual to be sure that the ulcer was healing satisfactorily before discharge. One patient remained in the hospital twenty-one days with vomiting, and the situation was complicated by the repair of a hiatus hernia; yet roentgen studies did not show inordinate obstruction of the pylorus.

The incidence of pulmonary complications of a major sort has been low. The best single index of the presence of such complications may be found in the postoperative elevation of temperature. In this group of 74 patients there were 7 who had elevations of temperature to 103 F. or higher during the first few postoperative days. In all instances these elevations were due to atelectasis with attendant pneumonitis; none of the patients had wound sepsis or empyema. Three patients were subjected to bronchoscopy because of the presence of bronchial mucus of a tenacious sort which the patients were unable to expectorate. Whenever it was used, bronchoscopy was effective in controlling these symptoms. In the past year virtually all the patients have received

prophylactic treatment with penicillin postoperatively, discontinued on the fourth or fifth day if the temperature remained normal or if the temperature had returned to normal by that time. It is conceivable that this use of penicillin tends to mask some of the pulmonary complications which otherwise might produce a febrile course. In no patient has an intrathoracic complication of any lasting significance developed. Three cases of pneumothorax requiring repeated taps for two or three days have occurred, presumably due to a small alveolar leak where adherent lung has been freed.

If care is taken in dietary management, the prolongation of hospitalization due to poor emptying of the stomach need constitute only a minor problem. As a cause for excessive hospitalization, it has been unimportant in this series (7 cases out of 74). One patient, mentioned earlier, had a true acute dilatation of the stomach with falling chloride level and rising levels of nonprotein nitrogen. Treatment by resumption of gastric suction sufficed to reestablish satisfactory emptying. In another case, considered a borderline case of pyloric obstruction, the patient was advised preoperatively of the possible necessity for a second stage to the procedure, was not able to establish a satisfactory diet and had a posterior gastroenterostomy carried out before discharge. Other patients with partial obstruction have been treated by subtotal gastrectomy rather than by resection of the vagus nerves, and until more adequate follow-up is available on the patients with gastrojejunal stomas treated by resection of the vagus nerves that will be the future policy.

Postoperative bleeding presumably of ulcer origin has occurred within two weeks of operation in 2 patients who were operated on because of previous hemorrhage, quiescent at the time of operation. The cause of bleeding in the early postoperative period following resection of the vagus nerves in patients with bleeding ulcers may stem from various sources. It is conceivable that the relaxed smooth muscle of the intestinal wall which ensues after this operation permits an increased blood supply which might well reflect itself in bleeding. It is also to be emphasized that the healing of an ulcer after resection of the vagus nerves takes a definite period of time and that if a vessel should happen to be transiently opened during this period of healing, bleeding might ensue, as it might in the healing of any other open wound. The hospital mortality in resection of the vagus nerves for ulcer has been, in our experience to date, zero. Among the early cases a patient who was suffering from diffuse gastric atrophy, rather than ulcer, was operated on and succumbed. This case has been mentioned in a previous publication.[1a] One patient died about nine months postoperatively of a cerebral vascular accident. Necropsy showed the ulcer to be satisfactorily healed. This case has likewise been previously reported and discussed in some detail [1b] and does not constitute a postoperative hospital mortality.

IV. COMMENT

The clinical results in this series may be summarized by stating that 87 per cent of the patients have had good results and are well satisfied with their operation two to thirty months postoperatively. Five patients have had a frankly poor result, either with a demonstrable recurrence (eighteen months postoperatively) or symptoms of ulcer. Five other patients have had sufficiently severe side effects consisting of diarrhea or other gastrointestinal manifestations so as materially to detract from their result. It is worth observing that some of these patients may later achieve a better gastrointestinal adjustment to the operation and at some later date be well satisfied with their procedure.[2]

From a technical point of view, there are two important features of this series. First, that all but 1 of the patients have been operated on through the thorax. Second, that only two postoperative posterior gastroenterostomies have been necessary.

In regard to the first point, of the 73 thoracic operations, 40 patients stated (in response to a questionnaire) that they had no discomfort of the chest at all after the first few postoperative days; 31 stated that there was minor discomfort, and only 2 have had major chest or intercostal pain, and both these patients are well at the present time. This would seem an adequate refutation of the argument that abdominal vagotomy should be performed so as to avoid difficulties from the chest incision.

The comparatively few gastroenterostomies necessary in this series may be due to the postoperative management of the stomach. This management extends throughout the first four postoperative months and consists essentially of giving the stomach an easy mechanical job to perform and of allowing it a complete twelve to sixteen hour rest, if the presence of fulness or diarrhea makes clear its protest. Many patients have thus been "tided over" a bout of motility symptoms, and they have remained well subsequently. There is a strong temptation to carry out gastroenterostomy under these circumstances; it is our conviction that it usually can be avoided.

Two patients who had frank obstruction preoperatively have been dealt with by gastroenterostomy and resection of the vagus nerves. In one case a preliminary gastroenterostomy and in another case a simultaneous gastroenterostomy were carried out. Both these patients were operated on for purposes of special investigation, as we are hesitant to inflict gastroenterostomy on these patients unless it is absolutely necessary. It is of the greatest importance to observe the patients with a gastrojejunal stoma for a longer time before being confident that no jejunal ulceration will occur or reoccur.

The 19 patients in this series who have had gastrojejunal stomas either primarily or secondarily have the same incidence of diarrhea and

fulness as have the series of patients with duodenal ulcer. This again has dissuaded us from performing many gastroenterostomies. As a treatment for frank obstruction it is effective; as a means of avoiding gastrointestinal side effects it is ineffective.

V. SUMMARY

The operative technic, postoperative management and hospital morbidity and mortality in a series of 74 patients with ulcer treated by resection of the vagus nerves have been reported. The thoracic approach has been used in 97 per cent of the cases.

Gastroenterostomy has been necessary postoperatively to relieve symptoms of obstruction in 2 cases—3 per cent of the series. In 2 other cases with frank cicatricial obstruction, primary gastroenterostomy was performed either before or with the resection of the vagus nerves.

It is hoped by the infrequency of gastroenterostomy to maintain this clinical experience in a state which will permit us, some years hence, to draw definitive conclusions about the value of resection of the vagus nerves. These conclusions will be difficult to draw if the operation is confused by the routine performance of posterior gastroenterostomy or other local procedures on the stomach which, in themselves, affect the natural course of peptic ulceration.

CLINICAL EVALUATION OF COMPLICATIONS OBSERVED AFTER TRANSTHORACIC VAGOTOMY

K. S. GRIMSON, M.D.

G. J. BAYLIN, M.D.

H. M. TAYLOR, Ph.D.

F. H. HESSER, M.D.

AND

R. W. RUNDLES, M.D.

DURHAM, N. C.

THE CENTRAL Surgical Association's invitation to participate in this symposium on vagotomy as a method of treating peptic ulcer is welcome. Dr. Dragstedt and his associates [1] have revived interest in the clinical and physiologic effects of vagotomy and have made observations that clarify many aspects of the problem of peptic ulcer. Our studies were encouraged by him. Preliminary impressions of clinical effects and summaries of roentgenologic, physiologic, and chemical studies have been presented.[2] Detailed reports will be published by

Read at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 22, 1947.

From the Departments of Surgery, Roentgenology, Biochemistry and Medicine of Duke University School of Medicine.

1. Dragstedt, L. R., and Owens, F. M.: Supra-Diaphragmatic Section of the Vagus Nerves in Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53**:152-154, 1943. Dragstedt, L. R.; Palmer, W. L.; Schafer, P. W., and Hodges, P. C.: Supra-Diaphragmatic Section of the Vagus Nerves in the Treatment of Duodenal and Gastric Ulcers, Gastroenterology **3**:450-462, 1944. Dragstedt, L. R., and Schafer, P. W.: Removal of the Vagus Innervation of the Stomach in Gastroduodenal Ulcer, Surgery **17**:742-749, 1945. Dragstedt, L. R.: Vagotomy for Gastroduodenal Ulcer, Ann. Surg. **122**:973-989, 1945. Thornton, T. F., Jr.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves: Effect on Gastric Secretion and Motility in Patients with Peptic Ulcer, J. A. M. A. **130**:764-771 (March 23) 1946.

2. (*a*) Grimson, K. S.; Taylor, H. M.; Trent, J. C.; Wilson, D. A., and Hill, H. C.: The Effect of Transthoracic Vagotomy upon the Functions of the Stomach and upon the Early Clinical Course of Patients with Peptic Ulcer, South. M. J. **39**:460-472, 1946. (*b*) Ruffin, J. M.; Grimson, K. S., and Smith, R. C.: The Effect of Transthoracic Vagotomy upon the Clinical Course of Patients with Peptic Ulcer, Gastroenterology **7**:599-606, 1946. (*c*) Smith, R. C.; Ruffin, J. M., and Baylin, G. J.: The Effect of Transthoracic Vagus Resection upon Patients with Peptic Ulcer, South. M. J. **40**:1-10, 1947. (*d*) Grimson, K. S.; Baylin, G. J.; Taylor, H. M.; Hesser, F. H., and Rundles, R. W.: Transthoracic Vagotomy: The Effects in Fifty-Seven Patients with Peptic Ulcer and the Clinical Limitations, J. A. M. A. **134**:925-932 (July 12) 1947.

individuals of the group, and the subject for this symposium will be only a brief clinical summary. No attempt will be made to review the literature or the recent excellent studies by Moore and his associates,[3] Machella, Hodges and Lorber,[4] and others.

Fifty-seven patients with refractory or frequently recurring peptic ulcer were treated by transthoracic vagotomy or transthoracic vagotomy and gastroenterostomy from July 1944 through September 1946. The transthoracic approach has been employed to minimize the chance of incomplete operation or of regeneration. The result in each patient has been determined by questionnaires, office visits and, with one exception, reexamination in the hospital. There was 1 death seventeen days after combined vagotomy and gastroenterostomy due to rupture of the stomach after an acute gastric dilatation and later a terminal massive hemorrhage from a duodenal ulcer.

Twenty-one of the remaining 56 patients are completely satisfied with the results of operation, 27 almost completely satisfied, 7 only partially satisfied and 1 dissatisfied because of an exacerbation of a preexisting gastrointestinal disturbance with vomiting and diarrhea.[4a] The major causes of complete or almost complete satisfaction have been relief from pain, vomiting or hemorrhage and ability to eat a less restricted diet. Fifty patients have gained weight, with 21 regaining a weight equivalent to their greatest weight at any time before vagotomy. Nevertheless, serious difficulties have occurred in a few patients and moderately troublesome symptoms have developed in others.

The greatest difficulty has been occurrence of obstruction at the outlet of the stomach with retention of gastric content and dilatation. Obstruction may be caused by scar tissue but more frequently may be a result of abnormal function of the outlet of the stomach after removal of vagal control. Distention, accumulation of fluid and gas and loss of normal peristaltic pattern after vagotomy frequently make stomachs appear "atonic" during fluoroscopy. Intragastric pressures, however, as judged by balloon studies made after a twelve hour fast, have been increased by a few centimeters of water both immediately after vagotomy and one to two and one-half years later. Obstruction and retention have necessitated secondary gastroenterostomy in 5 patients, eleven to one hundred and five days after transthoracic vagotomy. Two others

3. Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, New England J. Med. **234**:241-251, 1946; Resection of the Vagus Nerves in Peptic Ulcer: Physiologic Effects and Clinical Results, J. A. M. A. **133**:741-749 (March 15) 1947.

4. Machella, T. E.; Hodges, H. H., and Lorber, S. H.: The Restoration of Gastric Motility by Urethane of B-Methyl Choline After Section of the Vagus Nerves for Peptic Ulcer, Gastroenterology **8**:36-51, 1947.

4a. This patient died two years after vagotomy.

are now having serious symptoms from gastric retention but are being treated with partial success by parasympathicomimetic drugs.

Since Dragstedt has now adopted subdiaphragmatic vagotomy and frequently combines it with gastroenterostomy and others are routinely combining vagotomy with subtotal gastric resection or gastroenterostomy, and since the relative merits of the combinations are discussed in the symposium, this report will describe separately results in 36 patients treated by transthoracic vagotomy alone and in 20 patients with vagotomy and subtotal resection or gastroenterostomy.

TRANSTHORACIC VAGOTOMY WITHOUT GASTROENTEROSTOMY

Thirty-two of the 36 patients with vagotomy alone had duodenal ulcer and 4 gastric ulcer. Nine of the 32 patients are completely satisfied with results of operation, 22 almost completely satisfied and 5 only partially satisfied. Complications and causes of partial satisfaction varied.

Vomiting occurred occasionally during the first several months after vagotomy but did not persist. A single episode of hematemesis occurred in 2 patients seventeen and thirty-seven days after operation. With the possible exception of 1 patient who stated that he had had tarry stools, there has been no further recurrence of bleeding. Mild pain similar to that formerly produced by ulcer occurred for several months in 1 patient and for twenty months but only after bouts of drinking in another. Episodes of moderately severe pain recurred in a third patient two months after operation and continued intermittently for twelve months, at which time an ulcer crater was demonstrated in the duodenum. Unexplained serious episodes of colicky abdominal pain occurred in this patient and in 2 others.

Twenty-eight of the 36 patients described a sensation of fulness after eating during the first three months after vagotomy, and this persisted in 11. Eighteen patients experienced foul eructations during the first three months. These were usually described as having a sulfurous odor as that of rotten eggs. Foul eructations have persisted in 10. Moderate swelling or distention of the abdomen was described during the first three months by 20 patients, and this persisted in 9. Moderately severe colicky abdominal pain described as "gas pains" occurred during the first three months in 7 patients and persisted in 5. Mild or occasional "lower bowel cramps" occurred in 16 patients and persisted in 8.

Before vagotomy there was a tendency toward constipation in most patients, and afterward either a normal bowel habit or a tendency toward soft and frequent stools. Of the 36 patients without gastroenterostomy, 20 had normal bowel habits after vagotomy, 4 moderate constipation, 11 a continuous or periodic looseness of stools and 1 a serious diarrhea.

TRANSTHORACIC VAGOTOMY WITH GASTROENTEROSTOMY

Of the 21 patients who had gastroenterostomy before, at the time of, or after vagotomy, 6 had marginal ulcers occurring after subtotal gastric resection, 3 marginal ulcers after gastroenterostomy, 2 gastroenterostomy just before vagotomy, 5 gastroenterostomy at the time of vagotomy and 5 gastroenterostomy after vagotomy. Since there was 1 operative mortality in this group, the number of patients followed is 20. Gastroenterostomies performed at the time of or after vagotomy often functioned poorly for many days or weeks.

Twelve of the 20 patients with vagotomy and gastroenterostomy are completely satisfied, 5 almost completely satisfied, 2 partially satisfied, and 1 dissatisfied. Complications and causes of partial satisfaction or dissatisfaction have varied.

Vomiting occurred infrequently during the first months after vagotomy and persisted only in 1 patient who had diarrhea and vomiting before operation. Hematemesis or tarry stools have not occurred. Mild pain similar to that formerly produced by ulcer recurred in 1 patient now observed twenty-one months. Pain followed bouts of drinking. Unexplained serious episodes of colicky abdominal pain occurred in 3 patients. One of them had had a stoma ulcer and had a nonfunctioning gastroenterostomy three months after vagotomy, a poorly functioning stoma with star-shaped mucosal folds resembling a healing ulcer at thirteen months and a better functioning stoma with less evidence of mucosal defect at twenty-six months, when the episode of colicky abdominal pain occurred.

Twelve of the 20 patients with gastroenterostomy described a sensation of fulness after eating during the first three months after vagotomy, and this persisted in 6. Eight patients experienced foul eructations during the first three months, and these persisted in 5. Moderate swelling or distention of the abdomen was described during the first three months by 7 patients, and this persisted in 5. Moderately severe colicky abdominal pain or "gas pains" occurred during the first three months in 6 and has persisted in 4. Mild or occasional episodes of "lower bowel cramps" occurred in 9 patients and persisted in 4.

The bowel habit of these 20 patients with gastroenterostomy was normal after vagotomy in 13. There were moderate constipation in 2 patients, continuous or periodic looseness of the stools in 2 and a serious diarrhea in 3.

COMMENT

The detailed physiologic, roentgenologic and chemical studies made on these patients have not been abstracted, since they are summarized in another publication.[2d] Also beneficial effects of vagotomy have not been developed, since they are generally recognized and since most patients are well satisfied with results of operation. With 1 exception ulcers have healed or become quiescent.

Complications related to thoracotomy have been reported.[5] Complications related to disturbances of gastrointestinal function have been presented as they occur in the group of patients treated by vagotomy alone and as they occur in patients having vagotomy and gastroenterostomy. These complications usually were not troublesome but occasionally were serious. Vomiting, hematemesis or mild pain like that of ulcer occurred occasionally in the group with vagotomy alone and rarely if at all in the group with gastroenterostomy. Symptoms of fulness after eating, foul eructations or swelling of the abdomen were more frequent during the first three months in the group with vagotomy alone, but thereafter occurred about equally in the two groups. Colicky abdominal cramps of a mild variety occurred equally in the two groups. The occurrence of normal bowel movements also was about equal. There was a greater tendency toward a moderate, continuous or periodic looseness of the stools in the group with vagotomy alone. In the group with gastroenterostomy there was a higher incidence of serious diarrhea. Complete satisfaction occurred more frequently among the patients with combined vagotomy and gastroenterostomy than among patients with vagotomy alone.

Since secondary gastroenterostomy was necessary in 5 of 41 patients originally treated by vagotomy alone, since 2 patients with vagotomy alone are at present having serious difficulty with gastric retention and require treatment by parasympathicomimetic drugs and since other complications may be somewhat more frequent in this group, it seems probable that vagotomy alone should not be used as a standard treatment for duodenal or gastric ulcer.[6] Use of parasympathicomimetic drugs, particularly "urecholine" (carbaminoyl-beta-methylcholine chloride) has offered preliminary encouragement as a treatment of some complications but has not as yet been fully evaluated. Vagotomy may be of greater value when combined with gastroenterostomy or when used for stoma ulcers developing after gastric resection or gastroenterostomy.

CONCLUSION

Transthoracic vagotomy alone should not be used as a standard treatment of duodenal or gastric ulcer. Vagotomy may be of value when combined with gastroenterostomy or when employed for stoma ulcer.

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5. Grimson, K. S.: Complications of Thoracotomy Observed During Operations upon the Sympathetic and Vagus Nerves, S. Clin. North America. **26**: 1108-1123, 1946.

6. Since this paper was presented the 2 patients receiving parasympathicomimetic drugs have had pyloroplasty. Also 2 of 8 additional patients treated by transthoracic vagotomy alone have had recurrence. In 1 a gastric ulcer was treated by resection five and one half months after vagotomy, and the other had a massive hemorrhage after ten months.

EFFECT OF VAGOTOMY ON DEVELOPMENT OF THE MANN-WILLIAMSON ULCER IN THE DOG

JAMES V. OLIVER, M.D.
CHICAGO

RECENT reports [1] showing the beneficial effect of vagotomy on peptic ulcer have been the stimulus for the experimental work herein reported. This investigation was conducted to determine: (1) the effect of preliminary vagotomy on the development of the jejunal ulcer in the dogs on which the Mann-Williamson operation was done and (2) the effect on formation of ulcer when the vagotomy was performed after the Mann-Williamson operation.

Exalto [2] was the first investigator to report the incidence of jejunal ulcer in the dog following gastrojejunostomy with drainage of the duodenal contents into the colon. In his conclusions, valid to this day, he attributed the jejunal ulcer to the action of acid gastric juice on the intestinal mucosa.

Mann and Williamson [3] performed an end to end gastrojejunostomy, draining the duodenal contents into the terminal part of the ileum approximately 25 cm. from the ileocecal juncture. These investigators observed a large number of dogs and made a thorough study of the origin and evolution of the resultant lesions. The characteristics of the jejunal ulcers produced by diverting the duodenal secretions to the terminal part of the ileum have been outlined by them as follows:

1. Peptic ulcer develops in almost 100 per cent of dogs operated on.
2. The time of ulcer formation varies; perforation may occur in ten days or the ulcer may not start to develop for three months.
3. Although the animals lose weight rapidly and progressively, the change in physical condition does not appear to be a primary factor in the development of the ulcer.
4. Operative trauma is not a factor in ulcer formation.
5. Impairment of blood supply is not a factor in ulcer development.
6. The ulcer is always found in the intestinal mucosa, distal to the anastomotic suture line (within 1 cm.), lateral and posterior to the central axis of the intestine.

From the Department of Surgery, University of Illinois College of Medicine.

Read at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 20, 1947.

1. Dragstedt, L. R.: Ann. Surg. **122**:973, 1945.
2. Exalto, J.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:13, 1911.
3. Mann, F. C., and Williamson, C. S.: Ann. Surg. **77**:409, 1923.

7. The ulcer is usually single.

8. Grossly and microscopically, the ulcer appears similar to the peptic ulcer in man.

9. The ulcers heal readily if protected from the acid gastric juices.

Consideration of the extensive experimental evidence on the factor of nutrition in the pathogenesis of jejunal ulcer following internal duodenal drainage indicates that the incidence of ulcer is not materially modified by altering the level of duodenal drainage into the ileum. Summing up the experimental evidence on the factor of acidity in the causation of jejunal ulcer in the dog on which the Mann-Williamson operation has been done, the following facts have been established: 1. There is a prolonged secretion of highly acid gastric juice following operation (histamine factor). 2. Development of the ulcer can be retarded by draining the duodenal contents into the stomach. 3. Incidence of formation of ulcer is reduced by simultaneous partial gastrectomy. 4. Chronic perforating ulcer develops even though the health of the animal is maintained.

The jejunal ulcer in the dog on which the Mann-Williamson operation has been done bears great similarity to the human peptic ulcer both macroscopically and microscopically, and conforms to the histologic description of peptic ulcer by Aschoff [4] in his postulates: "A chronic round ulcer or peptic ulcer is a classical round or nearly round sharply punched out lesion involving the mucosa and deeper layers with induration of the base, infiltration of the edges, terraced margins, the steps of the terrace representing smaller extent of destruction as the deeper coats are involved and healing by cicatrization. The lesion is usually single and found superior and posterior to the central axis of the bowel."

METHODS OF EXPERIMENTAL PROCEDURE

This investigation was divided into three experimental procedures. All animals were permitted to survive their life span following the Mann-Williamson operation alone for the control group, or the vagotomy and Mann-Williamson operation combined for the other experimental groups. On arrival from the dog pound, the animals were quarantined for a period of ten days; no special or therapeutic diets were used and no preoperative conditioning of the animal was instituted. Postoperatively, their diet consisted of milk for three days, after which they were fed the stock diet of "purina dog chow" and water. At no time, either before or after the operation, was any medication administered or therapeutic measures instituted to sustain the animal. Therefore the mortality was high, particularly among the less robust animals. At necropsy, the cause of death in those animals which succumbed

4. Aschoff, L.: Pathological Anatomy, ed. 7, Jena, Gustav Fischer, 1928, vol. 2.

within one week after the operation was found to be pneumonia, volvulus, herniation of abdominal viscera, leakage at the suture line and operative shock. These animals were not used in evaluating the results of the experiments, since it is obvious that these animals had succumbed to the immediate effects of the operative procedures and the results could serve no statistical purpose.

A. Control Series—Mann-Williamson Operation Only.—The first or control series consisted of 15 animals subjected to the Mann-Williamson operation for internal duodenal drainage performed as follows:

With the dog under anesthesia with morphine and with pentobarbital sodium given intraperitoneally, the skin of the dog was aseptically prepared and a midline incision made in the upper part of the abdomen. The duodenum was transected at its pyloric juncture and the distal stump inverted. The jejunum was transected slightly distal to the duodenal-jejunal flexure at the ligament of Treitz. The distal limb of the transected jejunum was anastomosed end to end to the pylorus and the proximal limb anastomosed end to side to the terminal ileum approximately 25 cm. from the ileocecal juncture.

In this control series A, 9 animals survived the Mann-Williamson operation. The experimental data herein analyzed are derived only from this surviving group.

B. Vagotomy Followed by the Mann-Williamson Operation.—In the second experimental group, or series B, vagotomy was first performed as follows:

With the animal under anesthesia with morphine and with pentobarbital sodium administered intraperitoneally, an incision was made in the sixth intercostal space of the left side of the thorax, the intercostal musculature incised and retracted, exposing the parietal pleura. Under positive pressure, the pleural cavity was then opened and controlled respiration maintained throughout the operation until the thoracic cavity was closed. After the left lung had been retracted cephalad and medially, the mediastinal pleura investing the esophagus was incised, thus mobilizing the esophagus and facilitating its delivery into the operative field. The right and left vagus nerves were then identified coursing caudad on each side of the esophagus and isolated by blunt dissection, and a segment of nerve trunk 2 cm. long was removed from each nerve, due care being exercised to extirpate all interlacing vagal fibers coursing from side to side around the perimetry of the esophagus. The chest was then closed with interrupted linen sutures.

After a recovery period of approximately two weeks, the Mann-Williamson operation as previously described was performed on those animals which survived the preliminary vagotomy. Twenty animals were operated on in this series, but only 5 survived both the preliminary vagotomy and the subsequent Mann-Williamson operation. Data only from the surviving groups are analyzed. The unduly high mortality rate among the animals in this series was partially due to an epidemic of disease of the upper respiratory tract which was prevalent at the time.

C. Mann-Williamson Operation Followed by Vagotomy.—In the third group, or series C, the Mann-Williamson operation was first performed. After a varying period of approximately four weeks, during which time the animals were under constant observation for symptoms pathognomonic of development of ulcer, supradiaphragmatic bilateral vagotomy, as described in the previous section, was performed.

This period of four weeks' time between the Mann-Williamson operation and the subsequent vagotomy was allowed to elapse because the control experiments suggested that the ulcer developed at about this time as indicated by symptoms of malaise, anorexia, diarrhea, bloody stool and the progressive moribund condition of the animal.

In this series 20 animals were used, of which 7 survived both the Mann-Williamson operation and subsequent vagotomy. Therefore I have evaluated data only from the surviving group.

RESULTS

A. Control Series—Mann-Williamson Operation Only.—After the Mann-Williamson operation for internal duodenal drainage, the experimental animals were able to maintain their normal state of nutrition for a period of one week to ten days, after which a gradual and progressive loss of weight developed. At death, some dogs exhibited up to 40 per cent loss of preoperative body weight, and the survival period for all animals averaged seven weeks from the date of operation.

In this control series of 9 experimental animals, 3 succumbed within an average period of three weeks' time, with death attributed to inanition. At necropsy, no ulcer was demonstrable. In these 3 animals, the loss of weight was rapid, progressive and severe, amounting to 50 per cent of their preoperative body weight. The survival period of the remaining 6 animals averaged eight weeks, with death attributed to perforated jejunal ulcer. The most frequent site of formation of ulcer was found lateral and posterior to the central axis of the jejunum, immediately distal to the anastomotic suture line. In this group of 6 animals, the loss of weight was gradual, amounting to 35 per cent of their preoperative weight.

The 50 per cent loss in weight with the short survival period of three weeks for the animals in the group in which ulcer did not develop contrasts sharply with the 35 per cent loss in weight and a longer survival period of eight weeks average for the animals in which ulcer developed. This observation might raise the inference that the animals without ulcer did not survive a sufficient length of time after the operation for an ulcer to develop and that had they been better able to maintain their nutritional state and survived longer, all ultimately might have had ulcers. I admit that this is probably true. The results in this control series are set forth in table 1.

B. Vagotomy Followed by the Mann-Williamson Operation. — In this series, the vagotomy was performed, and after an interval of two weeks to allow for recovery the Mann-Williamson operation was performed. At the second operation, pronounced atonic dilatation of the stomach and intestines was observed in all animals. The distention of the stomach in most instances was marked; the volume of the stomach had increased up to 800 cc. Food residue was found in the stomachs of all dogs in this series despite the withholding of food for twenty-four hours previous to operation. Vagotomy resulted in hypotonicity, hypomotility and dilatation of the gastrointestinal tract which was still evident two weeks after vagotomy.

Of the 5 animals in this series which survived the effects of both operations, 4 succumbed to the effects of perforated jejunal ulcer; the fifth dog (no. 38) at necropsy was found to have a jejunal ulcer which

TABLE 1.—*Control Series A: Mann-Williamson Operation Only*

Dog No.	Weight, Pounds	Date of Operation	Date of Death	Survival Time, Weeks	Loss of Weight, Pounds	Cause of Death and Comment
3	20	3/16/46	5/31/46	10	10	Perforated jejunal ulcer
4	23	4/ 5/46	6/22/46	11	7	Perforated jejunal ulcer
5	20	4/19/46	6/10/46	9	7	Perforated jejunal ulcer
6	29	4/26/46	5/24/46	4	9	Perforated jejunal ulcer
7	19	5/ 3/46	5/20/46	3	8	Inanition; no ulcer present
8	17	5/10/46	7/17/46	9	9	Perforated jejunal ulcer
10	16	5/24/46	6/22/46	4	6	Inanition; no ulcer present
16	30	7/12/46	8/ 8/46	3	9	Inanition; no ulcer present
• 39	29	10/ 5/46	10/30/46	4	12	Jejunal ulcer, not perforated; severe hemorrhage

Number of dogs..... 9
Number of dogs with ulcer..... 6
Incidence of ulcer..... 67%,
but the other 33 per cent (3 cases) died so early following operation that insufficient time had probably elapsed for formation of ulcer.

was not perforated. The vagotomy, including extirpation of all interlacing fibers, was found complete in all postmortem examinations. No evidence of regeneration of the sectioned vagi was noted. The site of the jejunal ulcer which developed in all animals in this series was lateral and posterior to the central axis of the bowel, approximately 4 to 6 mm. distal to the anastomotic suture line. Vagotomy failed to protect against development of the Mann-Williamson ulcer in the dogs in this series.

The results for this series, as noted in table 2, constitute an incidence of ulcer of 100 per cent. The survival time of the 5 animals ranged from two weeks to six weeks, or an average of three and one-half weeks from the date of the second (Mann-Williamson) operation. The loss in weight for this group averaged approximately 35 per cent of the preoperative weight and was fairly constant in all animals.

C. Mann-Williamson Operation Followed by Vagotomy.—In this series, the Mann-Williamson operation was performed first. After an

interval of four weeks to allow for development of ulcer, as previously discussed, bilateral vagotomy was performed in all surviving animals. Of the 7 dogs which survived both operations, all died within fifteen days following the second operation (vagotomy). Four of the 7 died of perforated ulcer fifteen, eight, eleven and eight days, respectively, following vagotomy. A fifth animal (no. 9) succumbed twelve days after vagotomy and at necropsy presented only a slight erosion of the jejunum, which might have represented a healing ulcer. The remaining 2 dogs died four days and one day after vagotomy; no ulcer was found. The time interval following vagotomy in these 2 animals would appear too short to assume that complete healing of the ulcer had taken place. It is probably more accurate to assume that an ulcer had not been present when the vagotomy was performed, seven weeks and four and one-half weeks, respectively, after the Mann-Williamson operation. The results in this series are not at all conclusive regarding the role of

TABLE 2.—*Series B: Vagotomy Followed by the Mann-Williamson Operation*

Dog No.	Weight, Pounds	Date of Vagotomy	Date of Operation	Date of Death	Survival Time, Weeks	Loss of Weight, Pounds	Cause of Death and Comment
19	16	7/31/46	8/16/46	9/ 6/46	3	5	Perforated jejunal ulcer
34	19	9/11/46	9/27/46	10/ 8/46	2	7	Perforated jejunal ulcer
38	20	10/ 5/46	10/15/46	11/25/46	6	9½	Jejunal ulcer
42	19	10/11/46	10/23/46	11/13/46	3	7	Perforated jejunal ulcer
44	18	10/18/46	10/30/46	11/16/46	2½	6	Large perforated gastric ulcer; jejunal ulcer also
		Number of dogs					5
		Number of dogs with ulcer					5
		Incidence of ulcer					100%

vagotomy in healing of the ulcer, but at least it can be stated that vagotomy did not exert any beneficial effect (from the standpoint of healing) in the 4 animals which succumbed to perforation of the jejunal ulcer.

The location of the perforation in all animals in this series did not differ from the location of the ulcer in the dogs in the other series; namely, the lateral and posterior segment of the central axis of the jejunum, 6 mm. distal to the suture line. The average loss in weight for the animals in this series approximated that of the animals in the other two series; namely, about 35 per cent of their preoperative weight. The incidence of development of ulcer in this series of 7 animals was 71 per cent as determined by autopsy. The vagotomy was found complete in all animals. The results for this series are set forth in table 3.

COMMENT

At first glance these data might be construed as experimental evidence against the indication or efficacy of vagotomy as recommended by Dragstedt. However, I have seen such remarkable benefit sustained

after vagotomy by patients with ulcer that I am inclined to discount completely the significance of these experiments as related to clinical experience. In spite of the fact that the Mann-Williamson ulcer might be considered to resemble the peptic ulcer in man, the discrepancy in results following vagotomy in man as compared to the results in the experiments with animals leads me to the conclusion that the pathogenesis of ulcer following the Mann-Williamson operation in dogs is different from that of ulcer in man.

The role of acid in the production of ulcer in man, and particularly in its incidence, appears to be too definite to be disputed, at least in my opinion. It is a well known fact, as shown by numerous investigators, that vagotomy in animals produces a definite decrease in the amount of acid and in the total volume of gastric secretion in the dog. How can the failure of protection against formation of ulcer in the

TABLE 3.—*Series C: Mann-Williamson Operation Followed by Vagotomy*

Dog No.	Weight, Pounds	Date of Operation	Date of Death	Survival Time After Vagotomy, Days	Loss in Weight, Pounds	Cause of Death and Comment
9	30	5/17/46	8/12/46	12	13	Inanition—erosion of jejunum
13	13	6/14/46	8/12/46	4	5	No ulcer, inanition; stomach dilated
17	22	7/19/46	8/29/46	15	10	Large perforated jejunal ulcer
24	21	8/ 9/46	9/ 6/46	8	9	Large perforated jejunal ulcer
25	26	8/ 9/46	9/ 9/46	11	14	Perforated ulcer of jejunum
29	21	9/ 4/46	10/ 3/46	1	7	No ulcer; stomach markedly dilated
30	12	8/30/46	10/ 5/46	8	4	Perforated jejunal ulcer
	Number of dogs					7
	Number of dogs with ulcer					5
	Incidence of ulcer					71%

dogs on which the Mann-Williamson operation had been done, as noted in these experiments, be correlated with the two supposed facts just mentioned? One is led to the obvious conclusion that the excess acid is not the sole cause of ulcer. There must be another factor of great importance. This factor might be contained in bile, pancreatic or duodenal secretion, or in all three, since in the Mann-Williamson operation all three secretions are diverted from their usual location just distal to the stomach, where experimental ulcers are found; it may be that some chemical in one or more of these secretions serves to protect against their formation. However, there is ample evidence to prove that none of these three possible factors is sufficiently potent alone to produce ulcers, since the elimination of bile from the intestinal tract (by obstruction of the common duct) or of duodenal secretion and pancreatic secretion (by resection of the duodenum in carcinoma of the head of the pancreas) does not produce ulcers in a significant number of patients.

The benefit of feeding extracts of duodenum and of the upper part of the jejunum to patients with ulcer as reported by Ivy [5] and his associates offers proof that the correction of one factor (exclusive of the acid factor) may relieve ulcer in man. On the other hand, the good results following vagotomy in patients with ulcer may be ascribed to correction of the hyperacid factor unless one assumes that it also corrects a physiologic error in the secretions from the liver, pancreas or duodenum.

SUMMARY

In the 9 control animals (series A) in which only the Mann-Williamson operation was performed, ulcer developed in 6 animals, constituting an incidence of 67 per cent. A further analysis of the results in the control series reveals that the 6 dogs in which ulcers developed survived an average of eight weeks from the date of operation and lost approximately 35 per cent of their preoperative body weight during this period. These data are contrasted with an average survival time of three weeks from the date of operation and an average loss in weight of 50 per cent of their preoperative body weight in those animals in which ulcers did not develop.

Mann and Williamson in a large series of animals noted formation of ulcers in 98 per cent of their experimental animals, the time of formation varying from ten days to three months from the date of operation. All dogs which survived four weeks or longer after the Mann-Williamson operation only, succumbed to perforated ulcer. Obviously, in the series herein reported it can be assumed that the 3 dogs in which ulcer did not develop might ultimately have had one had they survived longer and been better able to maintain their nutritional state.

In those experimental animals in which the preliminary vagotomy was followed in two weeks by the Mann-Williamson operation (series B) the incidence of ulcer in those animals which survived the effects of the second operation by two weeks or longer was 100 per cent. All died of perforated ulcer. This is a higher incidence of ulcer than in the control group. The average survival time for the animals in this series was three weeks, during which time the animals lost approximately 35 per cent of their preoperative body weight. The debilitating effects of the two operations combined with the irritating effects of gastric retention of food, occasioned by atonic dilatation, hypomotility and hypotonicity following vagotomy, might be construed as facilitating the earlier development of the ulcer in this series as contrasted with the time of development in the control series.

When the Mann-Williamson operation was followed in four weeks (at which time the ulcer was presumed to develop) by vagotomy (series C), the incidence of ulcer was 71 per cent. In 7 animals sur-

5. Ivy, A. C.: Gastroenterology **3**:443, 1944; Federation Proc. **4**:222, 1945.

viving both operations, 4 succumbed to perforation of the ulcer, fifteen, eight, eleven and eight days, respectively, after vagotomy. A fifth dog died twelve days after vagotomy and at necropsy exhibited a slight erosion of the jejunum which might have represented a healing ulcer. The remaining 2 animals which did not show an ulcer at necropsy died one and four days following vagotomy, an interval of time too short to assume that vagotomy might have beneficially produced complete healing. It is probably more correct to assume that in these 2 animals the ulcer had not been present when the vagotomy was performed.

The incidence of development of ulcer for each series is set forth in table 4.

TABLE 4.—*Incidence of Development*

	Number of Dogs	Number of Dogs with Ulcer	Incidence of Ulcer, Percentage
Control series A, Mann-Williamson operation only.....	9	6*	67
Vagotomy followed by Mann-Williamson operation.....	5	5	100
Mann-Williamson operation followed by vagotomy.....	7	5	71

* The other 3 dogs died so soon after operation that there may have been no opportunity for formation of ulcer.

CONCLUSION

Bilateral supradiaphragmatic section of the vagi failed to prevent the ulcer produced by the Mann-Williamson operation for internal duodenal drainage in the dog. Since I am convinced that vagotomy produces a definite benefit (at least temporarily) in patients with peptic ulcer, I conclude that the pathogenesis in the two types of ulcer is too different to allow any correlation of these experimental results with the clinical results of vagotomy in peptic ulcer. However, the results of these experiments do suggest that there is another factor besides the role of acid in formation of ulcer in man. Since bile and duodenal and pancreatic secretions are diverted from their normal location in the Mann-Williamson operation, this second factor could theoretically be contained in any of the three secretions mentioned.

9 South Kedzie Avenue.

DENERVATION OF THE STOMACH

Historical Review

JOHN T. SMALL, M.D.
ROCHESTER, MINN.

"Now good digestion waits on appetite
And health on both!"

Macbeth—Act 3, Scene 4.

STATISTICS show that the incidence of peptic ulcer has risen with the pace of modern living,[1] but also improved diagnosis has probably relabeled as peptic ulcer some of the gastric neuroses, dyspepsias and neuralgias of the stomach and visceral neuroses of the pre-Roentgen era.[2] The influence of the mind over digestion, however, was recognized by the ancients, and when the anatomists discovered that the tenth cranial nerve extended from brain to colon, the early observations seemed to have an anatomic basis.

The *Philosophical Transactions of the Royal Society of London,* first published in 1664, was in effect the first international organ for the dissemination of scientific information. One hundred and fifty years later, Benjamin Brodie published therein the first clearcut observations of the influence of the vagus nerves on the secretions of the stomach.[3] He had sectioned both nerves in the necks of 3 dogs and later killed the dogs with arsenic. He observed, however, that the embarrassment of respiration was interfering with his results. His fourth experiment is worth reviewing:

> Having made an incision in the abdomen of a dog, immediately below the short ribs, I divided by means of a bistoury, the stomachic ropes formed by the nerves where they are situated on the esophagus immediately above the cardiac orifice of the stomach. The wound was closed by sutures. The respiration was

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From the Surgical Service, Mayo Clinic, and under the direction of Dr. Waltman Walters.

1. Wood, W. Q.: The Treatment of Duodenal Ulcer, Edinburgh M. J. **52**:433-450 (Dec.) 1945.

2. Allbutt, T. C.: Visceral Neuroses, Being the Gulstonian Lectures on Neuralgia of the Stomach and Allied Disorders, Philadelphia, P. Blakiston, Son & Company, 1884.

3. Brodie, B. C.: Experiments and Observations on the Influence of the Nerves of the Eighth Pair on the Secretions of the Stomach, Phil. Tr., London **104**:102-106, 1814.

not in the least disturbed but was performed as frequently, and with as much ease, as under ordinary circumstances. The animal was afterwards inoculated in the thigh with the white oxide of arsenic, and he died in a few hours after the application of the poison with the ordinary symptoms except that there was no fluid evacuation from the stomach or intestines.

On dissection, the mucous membrane of the stomach and intestine was found inflamed. There was no watery or mucous fluid in the stomach or small intestine. There was a small quantity of mucus in the colon.

The result of this being the same as that of the former exp'ts we may conclude that the suppression of the secretion in all of them was to be attributed solely to the division of the nerves, and all of the facts which have been stated sufficiently demonstrate that the secretions of the stomach are very much under the control of the nervous system.

This early experimenter gave credit to previous unnamed workers. He also pointed out the limitations of his method but forecast its eventual solution:

It has been attempted by former physiologists to determine how far the nerves are necessary to secretion. The only method which can be devised of ascertaining by direct experiment whether the nerves are really necessary to secretion is that of dividing the nervous branches by which the glands are supplied, but this with respect to the greater number of glands is an experiment impossible to perform; and with respect to others cannot be executed without so much disturbance and injury to the other parts as must render it extremely difficult to arrive at positive results. Perhaps in future investigations, some circumstance may arise which will enable us to determine more satisfactorily this important physiological question.

Since the fundamental work of Brodie the influence of the gastric nerves has been investigated along the three principal lines of secretion, motility and conduction of sensation. Many animal species have been employed in the laboratory and many pathologic states of human beings have been treated by denervation of the stomach. The extent of the operation has varied in the hands of different workers from simple division of nerves to complete excision of all branches in a large region. The existence of so many variables calls for caution in the evaluation of such procedures and no doubt accounts for the bizarre and often conflicting results which are reported. At the present time many surgeons are employing interruption of the gastric nerve supply in an attempt to treat the primary disease or secondary effects of peptic ulcer. This is not a new concept in treatment but has been widely investigated and practiced in the past. The purpose of the present study is to acquaint the reader with these past and present studies which are relevant to the understanding and further evaluation of this procedure.

ANATOMY

The vagi lose their identity at the level of the roots of the lungs. Behind the roots of the lungs, on both sides, lies the pulmonary plexus.

From this plexus the vagi incline anteromedially to break up into a variable number of branches which cross communicate on the esophagus to form the so-called esophageal plexus. At varying levels above the diaphragm the trunks reform and enter the abdomen via the esophageal hiatus. Each trunk contains elements of both vagi in addition to sympathetic fibers. These trunks are properly called the "gastric nerves," and are the structures which are sectioned when neurectomy is performed at the level of the lower part of the esophagus. Babkin [4] has stated that mere morphology is no criterion of the mode of action of a nerve, for action depends on the adrenergic or cholinergic properties at the nerve ending. One group of investigators concluded that the vagi contain only sympathetic fibers below the ganglion nodosum,[5] whereas another stated that they are entirely parasympathetic in origin.[6] White and Smithwick [7] have stated rather bleakly that neurosurgical methods have failed to relieve such clinical conditions as hyperacidity and pylorospasm since the essential mechanism that controls digestion lies in the intrinsic plexuses of the gastrointestinal tract. It is well known that preganglionic fibers of the vagus and sympathetic nerves have extraordinary powers of regeneration, and Cannon [8] has reported cardioinhibitor fibers rejoining the heart even after the intrathoracic portion of the vagus nerve has been transplanted to a new position outside the ribs.

Latarjet [9] and Wertheimer,[10] Mitchell [11] and McCrea [12] have clarified the distribution of the extrinsic nerves of the stomach in man and

4. Babkin, B. P.: Secretory Mechanism of the Digestive Glands, New York, Paul B. Hoeber, Inc., 1944.

5. Kiss, F.: The Relation Between Vagus and Sympathetic in Vertebrates, J. Anat. **66**:153-156 (Jan.) 1932.

6. McSwiney, B. A., and Spurrell, W. B.: The Gastric Fibres of the Vagus Nerve, J. Physiol. **77**:447-458 (March 15) 1933.

7. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System: Anatomy, Physiology, and Surgical Applications, New York, The Macmillan Company, 1947, pp. 355-374.

8. Cannon, W. B., cited by White and Smithwick.[7]

9. Latarjet, A.: Résection des nerfs de l'estomac: Technique operatoire; Résultats cliniques, Bull. Acad. de méd., Paris **87**:681-691 (June 20) 1922; Note préliminaire sur l'innervation et l'enervation de l'estomac, Lyon méd. **130**:166-167 (Feb. 25) 1921.

10. Latarjet, A., and Wertheimer, P.: Quelques résultats de l'énervation gastrique, Prèsse méd. **2**:993-995 (Nov. 28) 1923.

11. Mitchell, G. A. G.: Nerve-Supply of Gastro-Esophageal Junction, Brit. J. Surg. **26**:333-345 (Oct.) 1938; A Macroscopic Study of the Nerve Supply of the Stomach, J. Anat. **75**:50-63 (Oct.) 1940.

12. McCrea, E. D.: The Abdominal Distribution of the Vagus, J. Anat. **59**:18-40 (Oct.) 1924; The Nerves of the Stomach and Their Relation to Surgery, Brit. J. Surg. **13**:621-648 (April) 1926.

other species, although this subject has been treated rather superficially in the modern textbooks of anatomy. All of these workers have shown that the gastric nerves do not reach the pylorus directly but end at the angle of the stomach. The pylorus is innervated by recurrent branches in the lesser omentum which are richly mixed with sympathetic fibers from the celiac plexus. Latarjet is responsible for the terms "nerves of the lesser curvature" and "nerves of the greater curvature" for the nerves which extend to the angle of the stomach. McCrea pointed out the large branch of the right gastric nerve, which invariably travels with the left gastric artery to the celiac plexus. Recently Bradley, Wilson, Walters and I reported our findings at necropsy in 111 cases on the distribution of the vagus nerves to the esophageal plexus and thence to the gastric nerves.[13] This work revealed no significant variation related to age, sex or pathologic state and indicated that complete subdiaphragmatic section of the gastric nerves was possible in more than 90 per cent of cases. We emphasized the need for some standardization of terminology and suggested the term "gastric neurectomy" for total or partial resection of the gastric nerves, "gastric neurotomy" for simple division and the use of "vagotomy" for unilateral or bilateral division of the distinct vagus nerves above the cardiopulmonary plexuses.

LABORATORY STUDIES

Many investigators have found that the anatomic distribution of gastric nerves in the rabbit, cat and dog, animals which often are used in study of gastric denervation, is remarkably similar to that in man. Pavlov[14] and later Babkin[15] showed that secretion of gastric juice was intermittent in the dog, whereas Carlson[16] has found that in man it is continuous even during fasting and may even be increased during sleep. This does not indicate any fundamental difference between the activities of gastric glands of man and dogs but rather verifies the fact that it is impossible to eliminate psychic stimuli in the human subject. On the other hand comparison of results of gastric denervation must be made cautiously, since many workers have employed this procedure for the experimental production of peptic ulcer. A frequent error is to apply

13. Bradley, W. F.; Small, J. T.; Wilson, J. W., and Walters, W.: Anatomic Considerations of Gastric Neurectomy, J. A. M. A. **133**:459-461 (Feb. 15) 1947.

14. Pavlov, I. P.: The Work of the Digestive Glands, translated by W. H. Thompson, ed. 2, London, C. Griffin & Company, 1910.

15. Babkin, B. P.: Die äussere Sekretion der Verdauungsdrüsen, Berlin, Julius Springer, 1914.

16. Carlson, A. J.: The Secretion of Gastric Juice in Health and Disease, Physiol. Rev. **3**:1-40 (Jan.) 1923.

the findings in the lower animals to man without the necessary reservations.

The stomach was long regarded as a mechanical mill for the mixing and grinding of food, such as the gizzard in birds, until Reaumur (1683-1757) and Spallanzani (1729-1799) both showed that gastric juice could digest meat in vitro. This finding shifted attention to the chemical aspects of gastric function where, perhaps unfortunately, it has remained. However, complete absence of the gastric juice may exist without apparent difficulty in digestion, and Best and Taylor have stated that the immediate factors responsible for the production of the various symptoms of gastric disease probably are always mechanical in nature.[17] Ten years after Brodie's discovery of the influence of nerve supply on gastric secretion Prout showed that the acid content of gastric juice was hydrochloride. In the same year Beaumont began his work with Alexis St. Martin.[18] The production of free mineral acid during the living process is encountered but rarely, and Claude Bernard[19] was among the first to investigate its origin in the mucosa of the stomach.

After Billroth and his school established gastrointestinal surgery on the heels of anesthesia and antisepsis a deeper understanding of the whole complicated story of digestion became necessary. Around the turn of the century Pavlov defined and demonstrated the phases of gastric secretion, and his experimental work on dogs is the basis of present knowledge. The variations of the Heidenhain and Pavlov pouches, with and without nerve supply, gave information concerning the role of the gastric nerves in the control of sensation, secretion and motility, and surgeons soon began to use this knowledge in the treatment of various afflictions of the stomach.

Although Brodie had proved experimentally that the gastric nerves exerted control over gastric secretion, it remained for Pavlov and his followers to show that there were at least three phases to this phenomenon. It was ushered in by the cephalic phase, which in turn could be eliminated by sectioning these nerves. Alley[20] and Babkin later showed that stimulation of the vagus nerves caused secretion of a juice

17. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 3, Baltimore, Williams & Wilkins Company, 1943, p. 717.

18. Cannon, W. B.: The Book of William Beaumont After One Hundred Years, Bull. New York Acad. Med. **9**:568-584 (Oct.) 1933.

19. Bernard, C.; Cours de physiologie générale du Muséum d'histoire naturelle; de la vie commune aux animaux et aux végétaux, Paris, J.-B. Baillière & fils, 1878.

20. Alley, A.: The Secretory Activity of the Gastric Mucosa in the Region of the Lesser Curvature, Tr. Roy. Soc. Canada **27**:71, 1933.

which was both high in pepsin and strongly acid and was largely secreted from the region of the lesser curvature, which is the usual site of gastric ulcer. Vineberg [21] also indicated that the same nerves influenced the secretion of mucus from mucous neck cells and the gastric epithelium. He also found that mucus was capable of neutralizing acid and was useful in the treatment of ulcer. The influence of the sympathetic nerves has not been clarified but is apparently inhibitory to these functions. Variations in the pepsin and acid content of the gastric juice occur with the taking of different foods or the emotional state of the animal and strongly point to the role of the higher centers in modifying the reflexes. Even the sight or smell of food may excite the cephalic phase of secretion, and Babkin has shown that this phase may appear at the regular mealtime of laboratory animals although no external stimulus is present.

The location of autonomic areas in the higher centers has been extensively investigated. Goltz [22] was able to induce sympathetic and parasympathetic effects in dogs which had been decorticated, and ample evidence indicates that there are no separate regions for sympathetic and parasympathetic outflow from the cortex of the brain. Cushing [23] was the first to record the frequent occurrence of duodenal ulcer in association with lesions of the midbrain, and the recent experimental work of Beattie,[24] Sheehan [25] and others has indicated discrete centers in the preoptic and anterior hypothalamic areas which control various autonomic functions.

Leubuscher and Schäfer [26] in 1894, Boruttau [27] in 1896 and Herzen [28] in 1897 sectioned the vagus nerves in various experimental

21. Vineberg, A. M.: The Activation of Different Elements of the Gastric Secretion by Variation of Vagal Stimulation, Am. J. Physiol. **96**:363-371 (Feb.) 1931.

22. Goltz, F.: Der Hund ohne Grosshirn: Siebente Abhandlung über die Verrichtungen des Grosshirns, Arch. f. d. ges. Physiol. **51**:570-614 (March 26) 1892.

23. Cushing, H.: Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C Thomas, Publisher, 1932; Peptic Ulcers and Interbrain (Balfour Lecture), Surg., Gynec. & Obst. **55**:1-34 (July) 1932.

24. Beattie, J.: The Relation of the Tuber Cinereum to Gastric and Cardiac Functions (A Preliminary Note), Canad. M. A. J. **26**:278 (March) 1932.

25. Sheehan, D.: The Autonomic Nervous System, in Luck, J. M.: Annual Review of Physiology, Stanford University, Calif., Annual Reviews, Inc., 1941, vol. 3, pp. 399-448.

26. Leubuscher and Schäfer, A.: Über die Beziehungen des Nervus vagus zur Salzsäuresekretion der Magenschleimhaut, Zentralbl. f. inn. Med. **15**:761-767 (Aug. 18) 1894.

27. Boruttau, H.: Weitere Erfahrungen über die Beziehungen des N. vagus zur Athmung und Verdauung, Arch. f. d. ges. Physiol. **65**:26-40 (Oct. 31) 1896.

28. Herzen, P.: Les causes de mort après la double vagotomie dans leur rapport avec les conditions de Survie, Paris, J.-B. Baillière & fils, 1898.

animals and noted failure of digestion when this principal parasympathetic pathway was disturbed. The discovery of the roentgen rays greatly stimulated both clinical and experimental investigation of digestion in general and the stomach in particular. In 1929 Hartzell [29] gave an excellent review of the work of McCrea, Latarjet, McSwiney and Stopford and others when he reported his observations on dogs in which the vagi were cut above and below the diaphragm. He confirmed the abolishment of the cephalic phase of secretion, the loss of tone and the increased emptying time in the denervated stomach of the dog. In 1931 Vanzant [30] reexamined Hartzell's dogs and found that secretion and acidity had returned almost to normal despite the fact that the nerves were completely divided and showed no evidence of regeneration.

In 1925 Lim, Ivy and McCarthy [31] pointed out that many of the variations in the results reported by different investigators up to that time might be explained by the fact that the branches of the vagus nerves had been sectioned at different levels and had produced various types of denervation. Koennecke [32] and Meyer [33] in 1922 also exhaustively reviewed the subject and cautioned against drawing conclusions from the denervation of stomachs of healthy animals and comparing them to the effects on the ailing organ in man. Greggio [34] and Durante [35] in 1916, Beaver and Mann [36] in 1931, Beazell and Ivy [37] in 1936 and Lium [38] in 1941 were able to produce gastroduodenal ulceration in

29. Hartzell, J. B.: The Effect of Section of the Vagus Nerves on Gastric Acidity, Am. J. Physiol. **91**:161-171 (Dec.) 1929.

30. Vanzant, F. R.: Late Effects of Section of the Vagus Nerves on Gastric Acidity, Am. J. Physiol. **99**:375-378 (Jan.) 1932.

31. Lim, R. K. S.; Ivy, A. C., and McCarthy, J. E.: Contributions to the Physiology of Gastric Secretion: I. Gastric Secretion by Local (Mechanical and Chemical) Stimulation, Quart. J. Exper. Physiol. **15**:13-53, 1925.

32. Koennecke, W.: Experimentelle Innervationsstörungen am Magen und Darm, Ztschr. f. d. ges. exper. Med. **28**:384-412 (March 23) 1922.

33. Koennecke, W., and Meyer, H.: Röntgenuntersuchungen über den Einfluss von Vagus und Sympathicus auf Magen und Darm, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **35**:297-323, 1922.

34. Greggio, E.: Des ulcères gastro-duodénaux, Arch. de méd. expér. et d'anat. path. **28**:533-590, 1916-1917.

35. Durante, L.: The Trophic Element in the Origin of Gastric Ulcer, Surg., Gynec. & Obst. **22**:399-406 (April) 1916.

36. Beaver, M. G., and Mann, F. C.: Production of Peptic Ulcer After Section of Gastric Nerve, Ann. Surg. **94**:1116-1118 (Dec.) 1931.

37. Beazell, J. M., and Ivy, A. C.: Chronic Gastric Ulcer Following Bilateral Vagotomy in the Rabbit and the Dog, Arch. Path. **22**:213-219 (Aug.) 1936.

38. Lium, R.: Peptic Ulcer and Diarrhea Following the Removal of the Prevertebral Ganglia in Dogs: The Antispasmodic Effects of Magnesium Sulfate, Pentobarbital and Atropine Sulfate, Surgery **9**:538-553 (April) 1941.

rabbit and dog by denervation. Knight,[39] Ferguson [40] and associates about 1934 found a condition in the cat and monkey which simulated cardiospasm in human beings after denervation was performed.[41] Such variable results justify an attitude of caution concerning the use of this procedure as a therapeutic measure.

CLINICAL USE OF GASTRIC DENERVATION

Jaboulay [42] in 1901 recorded the first deliberate denervation of the stomach in a human being for the purpose of relieving the lightning pains of tabes dorsalis. He reported good results from resection of the celiac ganglion, and his operation was based on the supposition that the afferent (sensory) fibers from the viscus led to this cell station (fig. 1*A*).

Exner and Schwarzmann [43] in 1912 and later used the abdominal approach and divided only the anterior (left) gastric nerve (fig. 1*B*). They also were interested in relieving lightning pains. They reported 20 cases with 1 death and good results in 50 per cent of cases. They noted atony of the stomach and pylorospasm and recommended simultaneous gastroenterostomy in order to avoid gastric retention and failure of digestion. Barron and Curtis [44] and more recently Weinstein [45] and associates have used this procedure in relief of complicated duodenal ulcer.

Bircher [46] in 1920 and 1921 performed denervation in order to relieve gastric pains of varied causation. He interrupted the nerve

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39. Knight, G. C.: Relation of the Extrinsic Nerves to the Functional Activity of the Esophagus, Brit. J. Surg. **22**:155-168 (July) 1934. Knight, G. C., and Adamson, W. A. D.: Achalasia of the Cardia, Proc. Roy. Soc. Med. **28**:891-897 (Jan. 2) 1935.

40. Ferguson, J. H.: Effects of Vagotomy on the Gastric Functions of Monkeys, Surg., Gynec. & Obst. **62**:689-700 (April) 1936.

41. Ochsner, A., and DeBakey, M.: Surgical Aspects of Carcinoma of the Esophagus: Review of the Literature and Report of Four Cases, J. Thoracic Surg. **10**:401-445 (April) 1941.

42. Jaboulay, M.: La chirurgie du sympathique abdominal et sacra, Zentralbl. f. Chir. **1**:227-228 (Feb. 23) 1901.

43. Exner, A., and Schwarzmann, E.: Tabische Krisen, Ulcus ventriculi und Vagus, Wien. klin. Wchnschr. **25**:1405-1406 (Sept. 19) 1912; Gastrische Krisen und Vagotomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **28**:15-52, 1914-1915.

44. Barron, L. E., and Curtis, G. M.: Effect of Vagotomy on the Gastric Motor Mechanism in Man, Arch. Surg. **34**:1132-1158 (June) 1937.

45. Weinstein, V. A.; Hollander, F., and Jemerin, E. E.: Vagotomy in the Therapy of Peptic Ulcer, Surg., Gynec. & Obst. **79**:297-305 (Sept.) 1944.

46. Bircher, E.: Die Resektion von Aesten der N. vagus zur Behandlung gastrischer Affektionen, Schweiz. med. Wchnschr. **50**:519-528 (June) 1920; abstracted, Arch. d. mal. de l'app. digestif. **11**:135-137, 1921.

supply of the lesser curvature by dissecting the omentum and stated that an advantage of this minor denervation was the lack of atony and the necessity for gastroenterostomy (fig. 1*C*). There was a controversy in the literature between Bircher and others who favored more radical types of denervation.

Stierlin [47] and Steinthal,[48] writing in 1920, both recommended a more radical operation than the one which Bircher used. In addition to denervation of the lesser curvature by removal of the omentum they

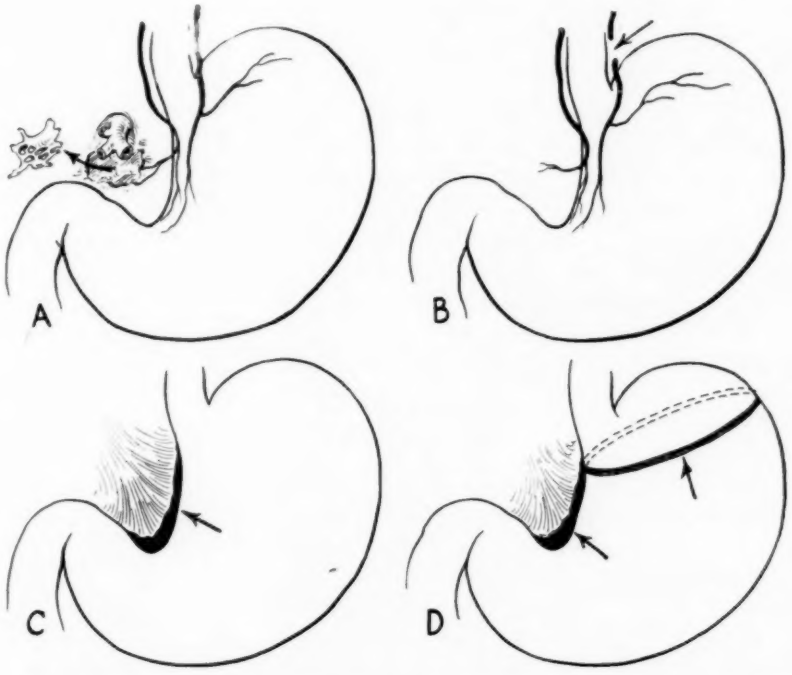

Fig. 1.—*A*, Jaboulay in 1901 excised the celiac plexus (schematic representation). *B*, Exner in 1912 divided the left gastric nerve (schematic representation). *C*, Bircher in 1920 used denervation of the lesser curvature (schematic representation). *D*, Stierlin in 1920 performed denervation of lesser curvature and circumcision (schematic representation).

incised the serosa and muscle down to the submucosa completely around the stomach at the level indicated in figure 1*D*.

47. Stierlin, E.: Ueber den Mageninnervation in ihrer Beziehung zur Ätologie und Therapie des Ulcus, Deutsche Ztschr. f. Chir. **152**:358-392, 1920.

48. Steinthal, C.: Die Ausschaltung des N. Sympathicus and N. vagus nach Stierlin bei Ulcus ventriculi, Zentralbl. f. Chir. **47**:1293-1294 (Oct.) 1920.

Latarjet,[9] Wertheimer,[10] Pauchet and associates,[49] after carrying out exhaustive experiments and anatomic investigations, evolved an operation which was performed in a total of 59 reported cases. Most of these operations were for ulcer of stomach or duodenum. In all but eighteen gastroenterostomy was required in order to drain the atonic stomach, and most of these eighteen operations were for "vagotonics without demonstrable lesions." Latarjet reported 1 case in which the patient returned in one year because of carcinoma which had developed

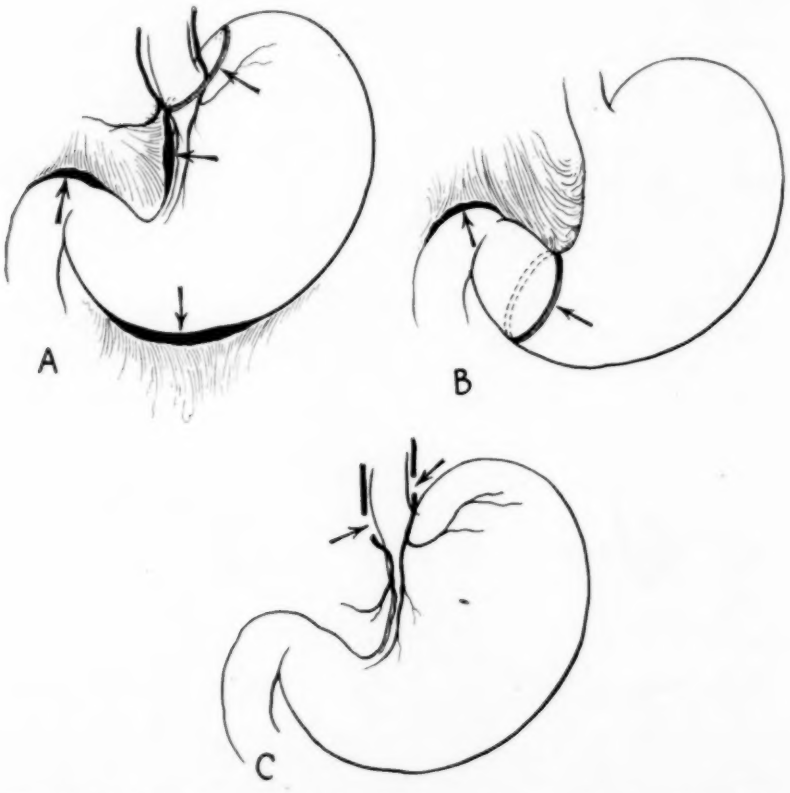

Fig. 2.—*A*, Latarjet in 1921 performed denervation of greater and lesser curvatures and suprapyloric region and partial circumcision (schematic representation of denervation). *B*, Schiassi in 1925 performed denervation of suprapyloric region with circumcision (schematic representation of denervation). *C*, Pieri and Tanferna in 1930 divided both gastric nerves (schematic representation).

without symptoms in the denervated stomach. The operation which this group used was designed to sever all the extrinsic nerves to stomach

49. D'Ormond, R. de B.: Neurectomy of the Stomach, in Pauchet, V.: Practical Surgery: Illustrated, translated by F. R. B. Atkinson, London, Ernest Benn, Ltd., 1925, vol. 6, chap. 3, pp. 41-52.

and pylorus and to leave intact the large branch of the right gastric nerve which accompanies the left gastric artery to the celiac plexus (fig. 2*A*). McCrea [12] in 1924 stated that the Latarjet operation was the one of choice for complete denervation of the stomach, without interruption of vagal supply to other organs.

Schiassi [50] in 1925 reported the results of a slightly modified operation in 26 cases. He incised the entire circumference of the stomach down to the submucosa at a low level and also divided the pyloroduodenal nerves which come down in the lesser omentum (fig. 2*B*). In 15 cases in which the operation was done for duodenal ulcer Schiassi was satisfied with his results. His work was published in American literature and he no doubt influenced such surgeons as C. H. Mayo,[51] who began stripping the omentum from the lesser curvature and pylorus to divide the pyloric nerves in order to relieve the symptoms of duodenal ulcer.

Pieri and Tanferna [52] in 1930 and Pieri [53] in 1932 divided both gastric nerves below the diaphragm (fig. 2*C*). They reported 8 cases of duodenal ulcer in which this operation was used without gastroenterostomy. This is the same operation, although probably less extensive, which was revived by Dragstedt [54] in 1943. Its use is now being reported frequently, but the results are rather conflicting.[55]

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50. Schiassi, B.: The Rôle of the Pyloroduodenal Nerve Supply in the Surgery of Duodenal Ulcer, Ann. Surg. **81**:939-948 (May) 1925.

51. Mayo, C. H.: Division of the Vagi for Pylorospasm, Ann. Surg. **88**:669-671 (Oct.) 1928.

52. Pieri, G., and Tanferna, U.: Studi sulla fisiologia dell'innervazione viscerale dell'uomo: II. Effetti della resezione del vago sulla secrezione gastrica, Riforma med. **46**:323-326 (March 3) 1930.

53. Pieri, G.: Bilateral Sub-Diaphragmatic Resection of the Vagus Nerves, Ann. ital. di chir. **11**:53 (Jan. 31) 1932; abstracted J. A. M. A. **98**:1950 (May 28) 1932.

54. Dragstedt, L. R., and Owens, F. M., Jr.: Supradiaphragmatic Section of Vagus Nerves in the Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53**:152-154 (June) 1943.

55. (*a*) Thornton, T. F., Jr.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves: Effect on Gastric Secretion and Motility in Patients with Peptic Ulcer, J. A. M. A. **130**:764-771 (March 28) 1946. (*b*) Dragstedt, L. R.: Some Physiological Principles in Surgery of the Stomach, Canad. M. A. J. **56**:133-137 (Feb.) 1947. (*c*) Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, New England J. Med. **234**:241-251 (Feb.) 1946. (*d*) Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Gastric Neurectomy for Gastric and Duodenal Ulceration, Ann. Surg. **126**:1-13 (July) 1947. (*e*) Colp, R., in discussion on Walters, W.: Vagotomy for Peptic Ulcer, Proc. Staff Meet., Mayo Clin. **22**:281-289 (July 23) 1947.

COMMENT

Wood has pointed out that peptic ulcer in the British Isles, as elsewhere, is steadily on the increase. He said that the incidence of perforation observed in hospitals of West Scotland had more than doubled from 1924 to 1941. During bombardments of World War II the incidence of perforation was particularly high, and he implied that this serves to emphasize the importance of psychosomatic factors in the causation of peptic ulcer. In reviewing the pathogenesis of gastroduodenal ulcer in 1942 Dragstedt reminded that section of the gastric nerves has long been practiced in the treatment of this disease but that the effects of the operation on continuous night secretion do not seem to have been investigated. Following his wide application of denervation over a three year period he stated: "Results are so satisfactory and the physiologic concepts back of the operation so appealing that I feel even at this early date warranted in recommending transthoracic section of the vagus nerves as a substitute for subtotal gastrectomy in the treatment of duodenal, jejunal and proved gastric ulcers." [55a]

Although Dragstedt has joined Sippy,[56] Winkelstein and others in the opinion that excessive night secretion is one of the great problems in treatment and that among patients with ulcer the amount and degree of acidity of this secretion are almost invariably more than normal, there is no universal agreement on this matter. Sandweiss, Sugarman, Podolsky and Friedman [57] recently have studied a group of normal persons and compared their results with those for a group of patients who had ulcer. Employing continuous suction they found acid juice in both groups at night regardless of ulcer diets, and only 1 patient with ulcer had a tendency to hypersecretion. Intermittent aspirations revealed greater volume of secretion among the patients with ulcer, which these workers have interpreted as simply meaning delay in gastric emptying.

Babkin and Karp [58] stated that whatever gastric hypersecretion may be—a cause or a symptom of peptic ulcer—it is evident that for therapeutic purposes it is most desirable to reduce the amount in patients with ulcer. They took a rather pessimistic view of the effectiveness of all forms of medical or surgical treatment at present and

56. Sippy, B. W.: Gastric and Duodenal Ulcer: Medical Cure by Efficient Removal of Gastric Juice Corrosion, J. A. M. A. **64**:1625-1630 (May 15) 1915.

57. Sandweiss, D. J.; Sugarman, M. H.; Podolsky, H. M., and Friedman, M. H. F.: Nocturnal Gastric Secretion in Duodenal Ulcer, J. A. M. A. **130**:258-265 (Feb. 2) 1946.

58. Babkin, B. P., and Karp, D.: Effect of Quinine and Atabrine on Gastric Secretion: A Preliminary Communication, Canad. M. A. J. **56**:137-141 (Feb.) 1947.

stated that the search for new drugs or surgical procedures to diminish secretory activity of the gastric glands is justifiable.

In spite of the low reported mortality for gastric denervation fatal results have occurred when the procedure has been used alone [59] or combined with sympathectomy.[60] Ulcers may progress and perforate silently into the peritoneal cavity,[61] or death may result from the usual complications of abdominal or thoracic operations. Disturbances of function were noted by many of the early workers in this field and have been reported on many occasions since 1937, when Adams and Phemister performed the first successful resection of the lower part of the esophagus, which involves also complete division of the gastric nerves. In such cases Churchill and Sweet mentioned the occurrence of tachycardia, sweating, gastric dilatation and atony, pylorospasm and sometimes an unexplained inanition without the presence of residual carcinoma.[62] All these symptoms, in addition to diarrhea, gastric retention, fulness, belching and physiologic obstruction whose tenure has been rather unpredictable, have been reported by various surgeons.[63] These disturbances of gastric motility have been the reason for the point of view that some form of drainage operation, such as gastroenterostomy or pyloroplasty, is necessary in many cases, and it is being employed routinely by many surgeons.

The abolition of any sensation of visceral pain by neurosurgical procedures is not fully understood at the present time,[64] and only a

59. Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Resection of the Vagus Nerves in Peptic Ulcer: Physiologic Effects and Clinical Results, with a Report of Two Years' Experience, J. A. M. A. **133**:741-748 (March 15) 1947.

60. Weeks, C.; Ryan, B. J., and Van Hoy, J. M.: Two Deaths Associated with Supradiaphragmatic Vagotomy, J. A. M. A. **132**:988-990 (Dec. 21) 1946.

61. Walters, W.; Neibling, H. A.; Bradley, W. F.; Small, J. T., and Wilson, J. W.: Favorable and Unfavorable Results of Gastric Neurectomy (Vagotomy) for Peptic Ulcer: An Anatomic, Physiologic and Clinical Study, S. Clin. North America **27**:885-904 (Aug.) 1947.

62. Churchill, E. D., and Sweet, R. H.: Transthoracic Resection of Tumors of the Stomach and Esophagus, Ann. Surg. **115**:897-920 (June) 1942. Sweet, R. H.: Transthoracic Resection of Esophagus and Stomach for Carcinoma: Analysis of Postoperative Complications, Causes of Death, and Late Results of Operation, ibid. **121**:272-284 (March) 1945.

63. Grimson, K. S.; Baylin, G. J.; Taylor, H. M.; Hesser, F. H., and Rundles, R. W.: Transthoracic Vagotomy: The Effects in Fifty-seven patients with Peptic Ulcer and the Clinical Limitations, J. A. M. A. **134**:925-932 (July 12) 1947.

64. Grimson, K. S.; Hesser, F. H., and Kitchin, W. W.: Early Clinical Results of Transabdominal Celiac and Superior Mesenteric Ganglionectomy, Vagotomy, or Transthoracic Splanchnicectomy in Patients with Chronic Abdominal Visceral Pain, Surgery **22**:230-238 (Aug.) 1947.

few reports have appeared. The individual response of the patient and the extent of the resection of the nerves are variables which have apparently complicated any evaluation of such results of gastric neurectomy.[65] The Hollander insulin test is the best available means of ruling out incomplete denervations in clinical data.[66] Many physicians feel that the loss of visceral pain is a disadvantage to the patient with ulcer who may be encouraged to exceed himself and to avoid proper medical surveyance. In certain patients who have undergone sympathectomy recrudescence of peptic ulceration has developed,[59] and progression of peptic ulcer also has been reported after vagotomy.[67] In the opinion of some surgeons this disturbance of autonomic balance between the sympathetic and parasympathetic nervous systems is not without hazard to the patient and also may account for the irregularity of reported results. It has also been suggested that vagal interruption renders hypertension more rapidly progressive.[59]

SUMMARY

The salient points noted on review of the literature may be summarized briefly as follows:

The results of experimental gastric denervation have been recorded for at least one hundred and thirty-three years, and gastric denervation in various forms has been employed for the clinical relief of pain, hypersecretion and hypermotility for about fifty years.

Vague terminology has confused the descriptions of surgical anatomy and surgical technic used in these procedures. Results of the operation on healthy animals of various species have been compared indiscriminately with those obtained by the operation on ailing human beings, and long term observations frequently have been contrasted loosely with immediate postoperative results.

Dragstedt and his followers have revived interest in gastric denervation and have instigated the first large scale evaluation of hundreds of clinical cases.

The indications for the operation have varied with the various series, and unfavorable results are apparently related to this factor.

65. Lehman, E. P., in discussion on Walters, Bradley, Neibling, Small and Wilson,[55d] Ann. Surg. **126**:1-18 (July) 1947.

66. Dragstedt.[55b] Hollander, F.: The Insulin Test for the Presence of Intact Nerve Fibers After Vagal Operations for Peptic Ulcer, Gastroenterology **7**:607-614 (Dec.) 1946.

67. Hallenbeck, G. A., and Priestley, J. T.: Transthoracic Vagotomy: Notes on Unsatisfactory Results in Two Cases, Proc. Staff Meet., Mayo Clin. **22**:332-336 (Aug. 6) 1947. Warren, R.: Experiences with Vagotomy for Peptic Ulcer, with Report of an Unsuccessful Case, Surgery **22**:246-258 (Aug.) 1947.

Gastroenterostomy and pyloroplasty are employed frequently as drainage operations in combination with the operation. They are designed to combat the attendant hypomotility of the stomach, especially when organic pyloric obstruction exists.

In the literature reviewed it was generally agreed that gastric denervation is efficacious in the treatment of gastrojejunal ulceration, but there is no general agreement concerning the direct loss of sensation of visceral pain which follows division of the gastric nerves. These effects have been ascribed to reduced motility of the stomach and also to interruption of sympathetic afferent nerves.

The Hollander insulin test is a reliable but not infallible means of demonstrating complete division of the gastric nerves. The use of this test has clarified clinical investigation in ruling out inadequate resections.

In addition to the treatment of peptic ulceration, gastric denervation has been employed with satisfaction in the treatment of intractable pain from chronic pancreatitis and carcinomatosis. Fatal results have followed the operation in hypertensive patients and after sympathectomy.

Insufficient time has elapsed to indicate the permanency of the favorable and unfavorable results of this operation and its proper place in the therapy of peptic ulcer.

DISCUSSION OF PAPERS ON PEPTIC ULCER

DR. MORTON GROSSMAN, Chicago: I should like to call attention to the pronounced difference in the results with oral administration of enterogastrone as reported by Dr. Ivy and myself and as reported by Dr. Saltzstein. Twenty dogs on which the Mann-Williamson operation had been done were treated by the oral administration of enterogastrone, and in 5 of these dogs jejunal ulcers developed: another 10 dogs have died in an average of nine months without formation of ulcer after operation; 5 animals are still alive at an average of eighteen months after operation. After the treatment had been carried out for nine months it was discontinued, so the animals now living were treated for nine months and have gone nine months without treatment and have not contracted ulcer in that time. I cannot offer an explanation for the discrepancy in these results, but I should like to offer some suggestions as to where the cause of the discrepancy might lie.

We used a different diet, which included raw pancreas and liver, for the dogs on which the Mann-Williamson operation had been done. This provides a means of counteracting the nutritional deficiencies which these dogs suffer because of diversion of the pancreatic jtice. This may be a factor of importance because the animals may not be able to survive long enough without such nutritional supplement for the action of the enterogastrone to occur. We are not able to test the efficacy of each batch of the material, and since it is a labile material the possibilities are that at times we use inactive material. We are at present devoting a great deal of energy to the development of rapid assay of each batch of material for its effect against formation of ulcer.

The beneficial effects of the administration of enterogastrone cannot be ascribed with certainty to the substance in it which depresses gastric secretion. The

effect against formation of ulcer is probably not caused by depression of gastric secretion. Nevertheless, inasmuch as in each case we have a substance which is able to manifest both activity against ulcers and secretory-depressant effects, until these have been isolated and shown to be separate substances, we cannot say that the effects are due to separate substances. No one has yet succeeded in preparing an extract of urine or intestinal mucosa which is effective against experimental ulcer but which is devoid of gastric secretion–depressant activity.

DR. R. ARNOLD GRISWOLD, Louisville, Ky.: My personal experience with vagotomy is limited to 30 cases. The clinical results have been satisfactory. The procedure is still in the investigative stage, and those clinics that have facilities available should consider this as a research project and do more in the way of physiologic research than is being done in some places.

We have heard a great deal about acid today. This is really not what we mean. What is meant is the peptic power of the gastric secretion; that is, its ability to digest protein, even the protein of the gastric and duodenal wall. Gastric secretion caused by stimulation of the vagus nerve is a secretion high in hydrochloric acid and high in pepsin. Secretion stimulated by the hormone gastrin is a secretion which is high in hydrochloric acid but low in pepsin. I should like to suggest that peptic power be investigated more thoroughly than it has been. All of these studies are important in evaluating this new procedure and correcting any failures which we may have. The simple use of an ordinary test meal is not adequate if we are going to come to valid conclusions concerning vagotomy.

DR. JOHN B. HARTZELL, Detroit: In 1928 or 1929 a group of dogs was trained to swallow a stomach tube. They were given test meals and then the gastric contents were aspirated. Normal curves were obtained for free and total acidity and p_H values. The right and left vagus nerves were then cut above the diaphragm, and gastric analyses were made. In each instance the free and total acids were much lower with a corresponding rise in p_H values. Observations were made for eight months and the findings were rather constant. Two and a half years later these animals were reexamined and were found to have marked dilatation of the stomach, and in some cases the acid had returned. Similar observations have been made by other men.

Operations such as vagotomy have been performed for duodenal ulcer as far back as 1924. Vagotomy was not popular at that time because the surgeons feared gastric atony and dilatation following operation. Dr. Charles H. Mayo early did a partial vagotomy below the diaphragm with other operations on the stomach. I mention this as it might be of some interest as an indication of how this operation has progressed.

It has been a pleasure and a privilege to be present during the presentation of these papers. It is difficult, I think, at the present time to be certain just what our opinion will be about this procedure five years hence. Only time will tell.

DR. I. F. STEIN JR., Chicago: On the surgical service of Dr. Karl A. Meyer at the Cook County Hospital twenty-four patients with peptic ulcer for which surgery was indicated have had section of the vagus nerves. Most of these patients have had thorough preoperative and postoperative studies. The first 5 were tested for vagal continuity by means of the subcutaneous injection of insulin, but the results were inconstant. Nineteen patients have been tested with a modification of the Hollander test (intravenous injection of insulin). Three of 6 patients with transthoracic vagotomy have had incomplete section of the vagus nerves; one of thirteen transabdominal operations was incomplete. The Hollander test,

in which insulin is injected intravenously, has been modified by (1) simultaneous studies of gastric motility and (2) a one hour control period of basal secretion and motility before the insulin is given. Following vagotomy, the presence of spontaneous or insulin-induced hunger contractions of type 1, 2 or 3 is indicative of incomplete vagotomy. This test is particularly useful after vagotomy for marginal ulcer following gastric resection, for the acid response of the patients is usually inconstant.

Motility studies with a balloon in the stomach have confirmed the work of Machella and others that "urecholine" (carbaminoyl-beta-methylcholine chloride) increases gastric motility after complete section of the vagus nerves. Similar studies have shown that "doryl" (carbaminoylcholine) promotes marked but temporary increase in gastric motility after vagotomy when given subcutaneously (0.25 mg.). "Doryl" when given by mouth (2 to 3 mg.) usually increases gastric motility for an hour or more. Both "doryl" and "urecholine" are useful in the treatment of gastric retention following complete vagotomy.

DR. PAUL HARPER, Chicago: One point which I wish to comment on is that our series of patients differs from Dr. Moore's in the incidence of diarrhea following gastroenterostomy. After vagotomy alone, about 50 per cent of the patients had some sort of diarrhea, while after vagotomy plus gastroenterostomy, we noticed this in only 15 per cent. What the explanation is for the difference between our observations and those of Dr. Moore I am at a loss to say.

There is another side effect which we have encountered in 15 per cent of the patients on whom we have done gastroenterostomy. This is a symptom complex characterized by weakness, sweating and the feeling of faintness within a half-hour or so following a meal, which has been rather disabling in 3 cases. In 2 cases, it was accompanied by diarrhea following each meal, which was moderately distressing. We attribute this to the fact that a dumping stomach caused these reflex symptoms from sudden distention of the jejunum, and we feel that this might be a reason for leaning away from doing gastroenterostomy routinely with vagotomy.

In considering the evaluation of these patients postoperatively as to whether they have a complete vagotomy, we do not feel that any one test is completely reliable. We feel that the insulin test has great value when the insulin is given intravenously. We have been using this test for the past two years, using 16 to 20 units intravenously, and we always attempt to demonstrate a positive response preoperatively. We have found that, on repeating the insulin test and giving occasionally as much as 40 units intravenously, we can get positive tests in 96 per cent of our cases before operation. We have tried sham feeding, but this test, while more physiologic, is less reliable. Of the postoperative reduction of the quantity of hydrochloric acid that is put out in the night gastric aspiration seems the most reliable criterion. If the output of hydrochloric acid is not reduced after operation, it seems to us fairly certain that the patient did not get a complete vagotomy. The appearance of symptoms of gastric retention is not a good criterion of vagotomy, as these have occurred in patients with positive reactions to insulin tests. We feel that all these factors should be considered in trying to decide whether the patient has a complete vagotomy or not.

DR. WALTMAN WALTERS, Rochester, Minn.: I should like to congratulate Dr. Grimson on his excellent studies on patients who have undergone vagotomy. I have wanted to do this since the time I read his first article. That was one of the most complete studies on a current clinical problem that I have known. To that

now must be added these fine studies that Dr. Moore has carried out at the Massachusetts General Hospital.

Some of my studies have been incomplete because the insulin test was not made prior to and after vagotomy, so the results could not be compared. Dr. Grimson said many months ago that postoperative studies of motility are an important part of the investigation of the results of the operation. It seems to me that investigating surgeons must proceed cautiously in application of these studies to clinical problems.

I am concerned about certain symptoms which develop after operations for duodenal ulcer. I want to call attention particularly to the symptom complex which Dr. Harper described. These symptoms frequently are described as the vagotonic symptoms associated with a dumping syndrome. Quite obviously if the stomach is dilated a dumping syndrome—that is, the immediate passage of the gastric contents into the loop of the jejunum anastomosed to the stomach—is not present unless it can be demonstrated by roentgenoscopy. With the use of "urecholine," which stimulates peristalsis by means of the sympathetic nerves, we can offer a patient whose stomach is dilated after vagotomy a great deal of relief. We must admit that we do not know what causes the weakness, faintness and sweating that occur after vagotomy. Just before I left my office I had a letter from a physician concerning a case in which I performed vagotomy and in which a similar complex developed. I do not know what to do for the patient.

Apropos of new surgical methods of treating gastric and duodenal ulcer, Somerville, of India, has recommended ligation of the major arteries to the stomach. In a recent report published in the *British Journal of Surgery* he stated that the results have been commendable in 28 of 80 cases. Recently I reviewed an article in which gastric ulcer was produced experimentally in a high percentage of animals by ligating the gastric artery, so apparently the neurophysiology of the stomach, duodenum and intestine is not too well known. I think that for the present most of us should continue to use the recognized methods of surgical treatment for gastric ulcer. The superiority of vagotomy over other standardized procedures in the treatment of duodenal ulcer still has to be proved. Its greatest value, at present, seems to me to be in the treatment of recurrent ulceration, especially after partial gastrectomy and possibly after gastroenterostomy, especially if in conjunction with vagotomy the gastroenteric stoma is to be obliterated and the recurring ulcer removed.

Dr. Francis D. Moore, Boston: I think that there has been a great deal of useful information mentioned here and I wish to thank the essayists and discussers for a most interesting afternoon.

Dr. Hartzell's comments were most interesting. In fact it was his early study that influenced us to take up these studies before we knew of Dr. Dragstedt's work.

I heartily agree that there is no single test for determining the efficacy of vagotomy. The best maneuver is to do a careful resection with adequate surgical exposure, in a leisurely and thorough fashion. I am sure that all of us are going to miss fibers in some cases and have troubles as a result. But these difficulties will be at a minimum if all who do this operation approach it as an anatomic challenge, and carry out preoperative and postoperative studies of secretion. The "thirty minute vagotomy" is a real threat in this field, and we must do all that we can to discourage it.

Dr. Keith S. Grimson, Durham, N. C.: The excellent reports of the essayists and the interest of the discussers are appreciated. It has been suggested that

the insulin test is not a reliable index of the completeness of vagotomy. Under the conditions with which our tests have been run and at some time during a six hour period about one third of the patients exhibited an increase of free acid. Variations have also occurred in consecutive tests on the same patient. Alteration of the response to insulin has been observed after subtotal gastric resection without vagotomy. Evidence is therefore confusing except that patients may have an excellent result from vagotomy even though they respond to insulin hypoglycemia.

Conventional usage seems to have established the term vagotomy for both transthoracic and transabdominal approaches. This probably is not a misnomer, since the physiologic effect is produced by division of the nerve and evidently little altered by variations of technic designed to prevent regeneration. Our technic includes resection of long segments of the nerve, but unlike operations on the thyroid, pancreas or stomach, this does not add to the physiologic effect.

USE OF BUFFER THROMBIN IN THE TREATMENT OF GASTRIC HEMORRHAGE

A Preliminary Report

BYRNE M. DALY, M.D.
DETROIT

SINCE the first use of thrombin in clinical medicine [1] in 1939, it has been used under a variety of circumstances for the control of bleeding. It is now generally available commercially, and its successful use in any particular situation generally requires that it be applied with the use of technics which take into account the properties of thrombin and the nature of the bleeding and its location. Its clinical application in supportive therapy for bleeding of the upper part of the gastrointestinal tract has not been considered feasible because of the acidity of the stomach. Without special precautions this high acidity will not only prevent thrombin from clotting fibrinogen but will also destroy the thrombin. A simple and practical technic has been developed which overcomes this difficulty, and evidence has been obtained which shows that thrombin is useful in the control of gastric hemorrhages.

PROPERTIES OF THROMBIN

This powerful clotting agent acts in a natural manner to clot fibrinogen directly. The concentrates now available commercially will accomplish this in a few seconds. There is, however, interference with the rate of clotting in solutions more acid than p_H 6.5, and, in addition, at p_H 4.3 the enzyme is destroyed.[2] In alkaline solution there is a greater range of maximum activity than on the acid side of neutrality. The dried powder is stable for a period of years, but in aqueous solution full activity is maintained only a few days. Since thrombin is easily

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From the Departments of Physiology and Surgery, Wayne University College of Medicine.

1. Warner, E. D.; Brinkhous, K. M.; Seegers, W. H., and Smith, H. P.: Further Experience with the Use of Thrombin as a Hemostatic Agent, Proc. Soc. Exper. Biol. & Med. **41**:655-657 (July) 1939.

2. (*a*) Seegers, W. H.: Purification of Prothrombin and Thrombin: Chemical Properties of Purified Preparations, J. Biol. Chem. **136**:103-111 (Oct.) 1940. (*b*) Seegers, W. H., and Smith, H. P.: Factors Which Influence the Activity of Purified Thrombin, Am. J. Physiol. **137**:348-354 (Sept.) 1942.

destroyed by a variety of factors it could not be assumed to be stable in phosphate buffers or in the stomach of patients after successful neutralization of the acidity of the stomach.

METHODS

The first step in this work was concerned with the measurement of thrombin activity in seventh-molar phosphate buffer (20.4 Gm. of disodium phosphate [Na_2HPO_4] in 1 liter of water plus 1.95 Gm. of potassium dihydrogen orthophosphate [KH_2PO_4] in 100 cc. of water) at room temperature. The contents of one ampule of thrombin (bovine) topical [3] were dissolved in 30 cc. of this buffer, and the thrombin activity was then measured quantitatively by the method described by Seegers and Smith.[2b] Repeatedly the stability was found to be approximately the same as in isotonic solution of sodium chloride.

In order to show that the gastric contents could be buffered to a p_H required by the properties of thrombin, a total of 35 normal and hospitalized patients were studied.

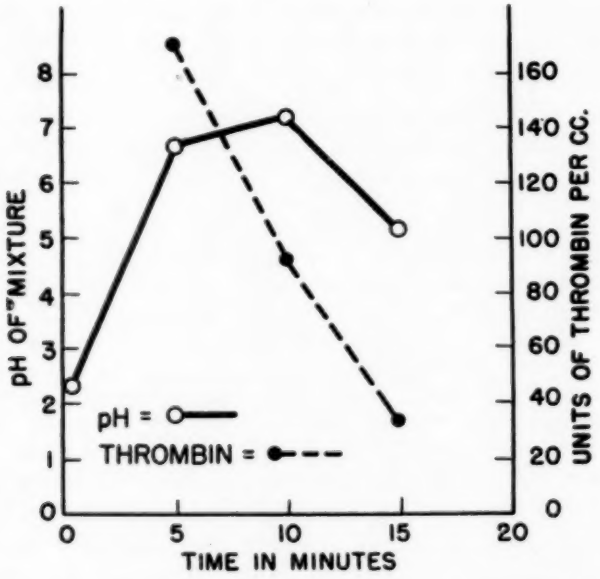
Within thirty to forty-five minutes of the noon meal, a Levine tube was passed and the contents of the stomach were aspirated with the patient lying on his left side. All this was discarded except 10 cc. which was retained as the initial specimen for p_H (Beckman, glass electrode) determination. Then 30 cc. of seventh-molar phosphate buffer was given by mouth, and after five minutes a specimen of 10 cc. was withdrawn to determine the p_H again. This then served as a measure of the efficiency of the buffer. Then 10,000 units of thrombin was dissolved in 30 cc. of the buffer, and this was given by mouth. A small specimen was then immediately taken for thrombin analysis. Exactly five minutes later a specimen was again taken. Its acidity was measured and the thrombin activity was also measured. Five minutes later, the final specimen was taken and the same tests were made.

Of the 35 cases, it was found that 31 showed thrombin to be present five minutes after administration in concentrations ranging from 1 unit to 150 units per cubic centimeter. In 3 cases the thrombin was not present despite a rise in p_H to within the range of thrombin activity. The thrombin may have passed the pyloris. One case failed to show the usual strong shift in p_H, and the thrombin was destroyed. The chart shows the values for p_H and thrombin concentration for 1 of the subjects studied. It represents a selected case which I consider to be midway between my best and poorest result. This showed that the activity of thrombin, placed in the stomach, remains for a time sufficient for any blood with which it might come into contact to be clotted in a few seconds. If, then, the thrombin were to gain ascess

3. The thrombin (bovine) topical was prepared by Parke, Davis & Company.

to a bleeding point or locus of oozing the desired hemostatic effect could be anticipated.

Effective hemostasis with thrombin is secured by having blood clot quickly as it emerges from the tissues. The clot then becomes anchored in and on the tissue surface. It therefore seemed more important to have a high concentration of thrombin for at least a few minutes than to have active thrombin for long periods of time. There must of course be ample time for the thrombin to come into contact with an extensive portion of the stomach surface so as to increase the chances of its coming in contact with the site of bleeding wherever it might happen to be in any particular case.



At zero time a sample of gastric contents was obtained. Thirty cubic centimeters of seventh-molar phosphate buffer was then given by mouth. Five minutes later a small sample was aspirated for determination of p_H. Immediately 10,000 units of thrombin topical was given with 30 cc. of phosphate buffer. Then, and at five minute intervals, specimens were taken for analysis of thrombin and p_H.

My colleagues and I were curious to know how long thrombin activity remains in buffered gastric juice. Three specimens were placed in the refrigerator at 8 C. for twenty-four hours. A loss of approximately 30 per cent of the total units of thrombin originally present was found. The result was more favorable than anticipated. Apparently the acidity of the gastric juice is the primary factor to be dealt with. This in vitro experiment cannot, of course, be interpreted to mean that thrombin would remain active in the stomach for twenty-four hours.

CLINICAL RESULTS

The patients treated were selected so as to represent only those who had a history of hematemesis with a definite picture of acute loss of blood. They had vomited blood prior to and/or during admission. The average hemoglobin value was 7.2 Gm. and the average red cell count 2,700,000. The patients were given 30 cc. of seventh-molar phosphate buffer, p_H 7.6, in order to neutralize and buffer the gastric contents. After five minutes this was followed by another 30 cc. of the buffer, containing 10,000 units of thrombin, or roughly 330 units per cubic centimeter.

Of the 21 patients treated 12 responded to the initial dose. They showed no further evidence of continued loss of blood. There was obvious improvement as shown by pulse rate, increase in blood pressure, increased red cell count and other clinical signs during an average of eleven and one-half days of observation in the hospital.

Five patients responded only after two or more doses. The fact that they did not respond to the first dose was plainly to be judged from their continued distress and further vomiting, all of which subsided after more attempts to remedy the situation with thrombin. Then they showed general improvement.

Four patients failed to respond and were operated on. The following observations were made: The first patient had pronounced hemorrhagic gastritis and esophageal varices. A clot of about 700 cc. was seen in the stomach. The second patient had a duodenal ulcer, and the thrombin may not have reached the bleeding point. The third patient also had a duodenal ulcer, which had eroded into the pancreas. The bleeding vessel was large and required ligation during the surgical procedure. The fourth patient had massive esophageal varices and advanced cirrhosis of the liver.

With a problem of this nature it is obviously difficult to evaluate the effectiveness of the new procedure. Thus far I have stated that thrombin can be recovered from the stomach and that there are good reasons for judging that thrombin was effective in 17 out of 21 patients. For further orientation it seemed appropriate to select, at random, from the records of the same hospital, 21 patients with bleeding ulcer not treated with thrombin. This was done and according to these records 10 patients showed no evidence of bleeding after admission, 10 showed continued episodes of bleeding, and 1 died of hemorrhage.

It is well known that bleeding peptic ulcers are variable in the amount and frequency of loss of blood. This uncertainty presents a definite hazard. Were it not for the fact that evidence of arrest of hemorrhage followed shortly after the administration of the buffer thrombin solution it might be argued that those patients in whom there was no subsequent bleeding might not have bled any more even without

treatment. A much larger series of patients would be necessary definitely to establish this point, but we believe that in this group of cases excessive losses of blood have been prevented by a simple and harmless procedure.

SUMMARY

From the clinical and laboratory experience gained so far, it is concluded that thrombin is definitely an aid in the control of gastric hemorrhage when the content of the stomach is buffered. Both the buffer and the thrombin are palatable and are nontoxic. It is realized that a series of patients is necessary for a thorough evaluation of this treatment, and the work is being continued. Heavy arterial bleeding and bleeding which ordinarily requires a ligature cannot be controlled by this substance alone. When thrombin does not alleviate gastric hemorrhage after four or five doses, it is felt that immediate surgical intervention is indicated.

This work was aided by a grant from the National Institute of Health. E. A. Sharp supplied the thrombin used in this work, and Arnold G. Ware, Charles G. Johnston and Walter H. Seegers gave technical assistance and made helpful comment.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1945

A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons

XXII. AMPUTATIONS, APPARATUS AND TECHNIC

Prepared by

J. WARREN WHITE, M.D., GREENVILLE, S. C., and CHARLES J. FRANKEL, M.D. CHARLOTTESVILLE, VA.

THE SAME trend toward discussions of acute trauma in orthopedic literature has continued in 1945 as in the previous war years especially as regards amputations and to a somewhat less extent fractures, for obvious reasons. In this section of the "Progress" as many articles on amputations were published as those on both apparatus and technic, the other two subtitles in our assignment.

Relatively few old line orthopedic articles appeared until well into 1946; these will be reviewed in next year's "Progress." A great many of these articles originated in military circles, where many of our more talented surgeons have been serving for several years and have gained special experience which will be of real value in civilian life. Next year there will be many less military articles as these men get out of uniform, but even so, many will be reporting their wartime experiences.

Amputations.—Most of the articles on amputations hew true to the line, but there are a few articles that depart from conservatism. Such a one [804] describes a routine amputation procedure in the mid thigh but leaves ¾ inch (1.9 cm.) of bone protruding from the purse-stringed closure. Apparently unmindful of the osteoclastic action at the level of the skin, this author was hoping to attach a prosthesis early to this bony projection and start immediate end bearing. He closes with the comforting statement that "further study will be necessary to determine how the skin and bone will react to each other and the new conditions." The only amputation reported in this brief article of this nature was on a rabbit.

The painful phantom limb syndrome was discussed at least four times, all the authors advising against further local surgical treatment without

804. Citron, R. R.: New Method of Amputation and Fitting of Prosthesis, Peoria M. News **16**:13 (March) 1945.

thorough study [805] and most of them concluding that the symptoms were of central rather than peripheral origin.

In an excellent article by Randall, Ewalt and Blair,[805c] the psychiatric reactions of the amputee is discussed. While this phase of the problem does not strictly come within our scope, it is urged that the article be read in full. In addition to discussing the "phantom limb" in the usual manner, the authors divide the psychiatric reactions into three phases—the immediate or first postoperative period when the patient should feel grateful that his life was saved, the intermediate period, during the usual revision of the stump, when the patient is in doubt about the future (this the authors feel is the truly critical period) and the late or final reaction when the patient has adjusted himself or not psychiatrically to the rapid tiring of the member and inability to be on his feet for a long time. The authors urge the acceptance of these persons in a humane way by their associates and community.

The increasing popularity of ice anesthesia in amputations, particularly those involving diabetes and arteriosclerosis, is shown by the number of articles that continue to appear.[806]

Mock [807] reports a case in which a tourniquet was left on a refrigerated extremity for three and one-half hours because of unavoidable circumstances without deleterious effect on the tissues.

For any one particularly interested in ice anesthesia, the description by Cayford and Pretty [808] of the technic employed at the Montreal General Hospital is well worth reading. It is far simpler than the usual technic, and one of us has used a similar procedure several times with complete satisfaction.

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805. (*a*) Williams, G. A.: Phantom Limb Syndrome Complicating Pregnancy and Puerperium, Am. J. Obst. & Gynec. **50**:546-547 (Nov.) 1945. (*b*) Livingston, K. E.: Phantom Limb Syndrome: Discussion of Role of Major Peripheral Nerve Neuromas, J. Neurosurg. **2**:251-255 (May) 1945. (*c*) Randall, G. C.; Ewalt, J. R., and Blair, H.: Psychiatric Reaction, J. A. M. A. **128**:645-652 (June 30) 1945. (*d*) Herrmann, L. G., and Gibbs, E. W.: Phantom Limb Pain: Relation to Treatment of Large Nerves at Time of Amputation, Am. J. Surg. **67**:168-180 (Feb.) 1945.

806. Paterson, F. M. S.: Refrigeration Anesthesia in Diabetic Surgery, Proc. Am. Diabetes A. (1944) **4**:141-167, 1944. Dennis, C.: For Amputation of Thigh: Ice Anesthesia, Hospitals **19**:83-84 (Aug.) 1945. Melick, D. W.: Refrigeration Anesthesia, Am. J. Surg. **70**:364-368 (Dec.) 1945. Lam, C. R.: Refrigeration Anesthesia, Arch. Phys. Med. **26**:20-22 (Jan.) 1945. Shaar, C. M.; Jones, D. T., and Lehan, T. R.: Refrigeration Anesthesia, S. Clin. North America **24**:1326-1336 (Dec.) 1944. Jewett, E. L.: Skin Traction for Amputation Stump, U. S. Nav. M. Bull. **44**:629-632 (March) 1945.

807. Mock, H. E.: Refrigeration in Trauma: Report of Nine Year Old Patient with Lower Extremity Gangrene Following Dislocation of Distal Femoral Epiphysis, Am. J. Surg. **67**:424-435 (Feb.) 1945.

808. Cayford, E., and Pretty, H. G.: Refrigeration Anesthesia and Evaluation of Amputation Sites by Arteriogram, Ann. Surg. **121**:157-163 (Feb.) 1945.

Another excellent article of general interest on refrigeration in trauma of the extremities is by McElvenny,[809] who writes exhaustively on the subject and should be read by all who are interested. An excellent review of the literature is presented as well as practical points in the technic. Nothing, however, is brought out that has not been indicated in previous articles.

Most of the articles discussing the technic of amputations stress the need for the avoidance of excess muscle at the end of the stump and advise the cutting of the muscle at the level of the bone and wedging the inner cone leaving only deep fascia and skin to cover the bone ends. Another point that is justifiably mentioned in most articles discussing the technic is the necessity and value of skin traction.

The controversy about the treatment of nerve ends continues. Kirk's recent statement that there is no ideal way seems to hold true. In view of this, it seems to us that the best way is probably the simplest; i. e., the transverse severance of the nerve with a sharp scalpel an inch (2.5 cm.) or so proximal to the distal cut surface of the muscle. An enumeration of various ways of treating nerve ends at amputation is given by Metz,[810] who himself advocates ligation with chromic gut to control bleeding, severing the nerve speedily with a sharp knife.

Brown [811] discusses the details of the manufacturing of prostheses for the hand using "foamed latex mixtures." This is beyond the needs of the average orthopedic surgeon, but when one remembers this author's excellent exhibits at various medical meetings, one reads the article with much interest and is glad to know of someone to whom an occasional case may be referred.

For those surgeons interested in kinetic or cinematic operations, an encouraging article by Bartley [812] is cited. In one clinic mentioned where these cases were looked up, 83 per cent of 403 patients on whom this operation had been performed were using their artificial arms. In another clinic surveyed by Kessler, the chief advocate of this operation, only 12 per cent of 278 arm amputees, who did not have a kinetic arm, were wearing an artificial arm for cosmetic purposes only, and only 2 were wearing a mechanical arm for functional use. In Germany five years after World War I a review was made of the 7,000 hand and arm amputees, and it was found that only 1.8 per cent were wearing any sort of mehanical arm for functional use.

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809. McElvenny, R. T.: Refrigeration in Trauma of Extremities, S. Clin. North America **25**:192-209 (Feb.) 1945.

810. Metz, A. R., in discussion on Herrmann and Gibbs.[805d]

811. Brown, A. M.: Prosthetic Restorations After Amputations About Hand, Am. J. Surg. **68**:338-343 (June) 1945.

812. Bartley, S. P.: Kinetic Amputations and Plastic Reconstructions of Fingers: Operative Technic and Functional Results, Am. J. Surg. **67**:181-183 (Feb.) 1945.

This argues in favor of the kinetic amputations, but it must be conceded that the technic is above the ability of the average surgeon.

Realizing the tendency of the average patient to lay aside his arm prosthesis before he really knows how to use it, Olson [813] in a well written paper emphasizes the importance of prolonged instruction before the patient is allowed to be without supervision. This in civilian practice is much more difficult than in military or veterans' service. We believe that this author is incorrect when he states in this article that the waddling gait of a thigh amputee on a prosthesis is due to the weakening of adductor power. The reverse is really true, as the patient without the ability to abduct his limb because of the shortness of his stump has to put his center of gravity over this leg when he bears weight and the equivalent of a gluteus medius gait is the result. In general it is true that the longer the thigh stump is—as long as it does not include the condyles—in amputations above the knee, the better will a patient walk, everything else of course being equal.

Sugarbaker and Ackerman [814] feel that the major hind quarter amputation is not done as often as it should be and that the operation should depend more on the pathologic indications rather than the physical tolerance of the patient.

One paper on forequarter amputation was published by Berman,[815] who reported 5 cases. Three of the patients died within a year, and the other 2 were alive and well a year and a half after operation. A detailed description is given of the technic, which does not depart particularly from that employed by Pack.[816]

This year there seems to be a dearth of articles on prosthesis, suggesting that a general understanding has been reached by both the military and civilian makers of prostheses. As regards preparing a stump of a lower extremity, Stevens [817] has designed a simple harness apparently superior to the usual "shrinker" aimed particularly for developing muscles above the site of amputation. The article is well illustrated.

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813. Olson, P. F.: Amputation During the War and After, Surg., Gynec. & Obst. **81**:688-691 (Dec.) 1945.

814. Sugarbaker, E. D., and Ackerman, L. V.: Disarticulation of Innominate Bone for Malignant Tumors of Pelvic Parietes and Upper Thigh, Surg., Gynec. & Obst. **81**:36-52 (July) 1945.

815. Berman, J. K.: Interscapulothoracic Disarticulation of Arm, Surgery **18**: 256-266 (Aug.) 1945.

816. Pack, G. T.; McNeer, G., and Coley, B. L.: Interscapulothoracic Amputation for Malignant Tumors of the Upper Extremity: Report of Thirty-One Consecutive Cases, Surg., Gynec. & Obst. **74**:161-175 (Feb.) 1942.

817. Stevens, A. G.: Exercise Harness for Use of Lower Extremity Amputees, Physiotherapy Rev. **25**:27-29 (Jan.-Feb.) 1945.

Apparatus.—Once again, stimulated obviously by the opportunities of closer relationship between the surgeon and the brace shop in military service, many original pieces of apparatus have been devised and published officially from the various branches of our armed forces.

In relation to plaster technic possibly the most important device since the advent of the use of plaster of paris casts in the early 1850's has appeared on the market. The reciprocating electrical plaster cutter devised by Stryker has made the removal and fenestration of plaster casts a pleasure. The sole drawback experienced by one of us in using this truly marvelous instrument is the disquieting noise made by the reciprocating mechanism. A description of the instrument has not yet appeared in print, but most orthopedic surgeons have seen it on exhibit at the meetings of the Clinical Orthopedic Society and the Orthopedic Academy in October 1945 and January 1946, respectively.

The possibility of the use of this instrument to replace the dangerous rotating electric bone saw immediately occurs to the bone surgeon, and it is hoped that it will be available in the not too distant future. Stryker is working on that now.

A refinement of the valuable cast wedging idea has been published by Rhinelander and Ropes,[818] who describe three types of hinges for use in correcting articular deformities, particularly of the knee and the elbow.

The chief advantage of this apparatus is that the leather strap type of plaster hinge has been replaced in one instance by a steel strap and in the other two instances by conventional hinges, one being fitted for gradual correction with a turnbuckle arrangement. One of us has in the past gotten along rather well simply by using a small uncut portion of the cast as a hinge, but admits that in some of the more difficult problems this more formal idea would be of real value. The article is well illustrated.

Two more walking plates for attachment to plaster casts have been devised,[819] both rather similar and having the same two objectives—a weight-bearing surface that is less noisy and not so hard on floors and a convex rocker bottom arrangement for ease in walking.

The *Army Medical Bulletin,* publishing an article by Harvey,[820] describes a split drum for use in making plaster reenforcements, or

818. Rhinelander, F. W., and Ropes, M. W.: Adjustable Casts in Treatment of Joint Deformities, J. Bone & Joint Surg. **27**:311-316 (April) 1945.

819. Vineberg, A. M., and Murphy, D. R.: New Rocker Type of Cast Walker: Preliminary Report, Canad. M. A. J. **52**:394-397 (April) 1945. Koven, B., and Koven, M. T.: Walking Iron with Foot Plate, Am. J. Surg. **68**:270-271 (May) 1945.

820. Harvey, R. K.: Device for Making Plaster of Paris Reinforcements, Bull. U. S. Army M. Dept, June 1945, no. 89, pp. 118-119.

splints as they are sometimes called. With the satisfactory commercial product, this device is not so necessary now as it formerly might have been.

A description of an improved Tobruk plaster was published in the *Bulletin of War Medicine* [821] by the editorial staff. It is of little moment in peacetime, but might be of considerable value in an emergency.

Rowe [822] recommends the use of used roentgen film strips (6 by 1 inch [15.2 by 2.5 cm.]) to reenforce plaster casts. It is believed that others, including us, might express some doubt about this idea, as it is feared that the film strips are likely to weaken the plaster by preventing complete bonding together of all the layers of the plaster. It is mentioned here solely because the author is suggesting something which in his hands has been worth while. Possibly the emulsion on the roentgen ray film serves to bind the plaster and the film together.

Anderson and Erickson [823] have come out with another plastic cast, this time a combination of "fiberglas" and cellulose acetate with a setting fluid. It is strongly recommended, but one wonders whether it will be more successful than the "castex" product, which is still used to some extent. The porosity and waterproofing of the product and imperviousness to roentgen rays are factors decidedly in its favor. Its use as a routine clinic supply is prevented by its cost together with its somewhat increased difficulty of application. This is apparently the same material that was reported the year before in *Northwest Medicine*.[824]

With all their disadvantages, it is difficult to improve on the old time plaster bandages, particularly the commercial type put out the last few years. We have wondered, as have often many others during hot summer days, whether some sort of tubing might be incorporated between the layers of a hip spica so that ice water might be run through, and were much interested in reading an article by Cromar,[825] who has done this and considers it of value. Using perforated tubes and passing air through them, he mentions the possible use of an insecticide if found necessary.

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821. Improved Tobruk Plaster (Mark III), Bull. War Med. **5**:241-242 (Dec.) 1944.

822. Rowe, M. L.: Easy and Economical Method of Making Removable Casts, J. Bone & Joint Surg. **27**:521-522 (July) 1945.

823. Anderson, R., and Erickson, H. R.; Glass Plastic Cast, Am. J. Surg. **69**:299-305 (Sept.) 1945.

824. Anderson, R.: New Waterproof Plastic Cast, Northwest Med. **43**:365-371 (Dec.) 1944.

825. Cromar, C. D. L.: Body Cooler for Use with Plaster of Paris Casts. J. Canad. M. Serv. **2**:183-185 (Jan.) 1945.

A tentlike frame has been devised as a substitute for the time-honored Balkan frame. Its three originators [826] claim in addition to the usual merits of the latter apparatus that it can be used as an oxygen tent. Aside from this and that less overhead room is needed, there seem to be no special merits that are not shared by the Balkan frame. One disadvantage is that, with the pitched roof type of overhead cross members, at least two extra cross members are required.

Holman [827] has described a useful suspension bar for a Thomas splint when used on a stretcher. This supports as well as firmly stabilizes the distal end of the splint, adding materially to the safety and comfort of the injured extremity.

Spiegler [828] advocates a simplified humeral splint, the fundamental parts of which are two rectangular pieces of sheet metal of proper size and gage and a malleable metal strip. One metal plate supports the humerus and the other, when the malleable metal strip is attached to both, holds the arm abducted when pressed against the side of the body. Both, of course, are properly padded and fitted with stabilizing straps, but the manner of supporting the forearm is not discussed except to state that "a collar and cuff, or cravat sling, may be applied from the neck to the wrist." It occurs to us that this splint might well be incorporated into an arm plaster and thus take the place of the difficultly applied shoulder spica. One of the illustrations shows a rather distressing amount of internal rotation of the forearm which is bound to occur if the forearm is not properly supported.

Andreasen [829] describes a shoulder abduction splint using the Bohler Cramer wire properly bent and padded. This is similar in construction and use to the efficient splint originally described by Bohler which every once in a while should be brought to our attention. As an immediate postoperative dressing, adhesive tape being used instead of straps, it is most useful. As the patient convalesces the adhesive tape can be gradually replaced by straps.

In line with the suggestion, Phalen [830] incorporates a leg brace in a plaster spica for hip immobilization, particularly acetabular fractures. In his illustration, much more immobilization of the hip would have

826. Healy, W. V.; Peterson, C. A., and Chapman, E.: St. Clare Fracture Frame: Preliminary Report, Indust. Med. **13**:998-1000 (Dec.) 1944.

827. Holman, M. S.: Suspension Bar for Thomas Splint, Lancet **2**:434 (Oct. 6) 1945.

828. Spiegler, A. A.: Simplified Humeral Splint, Am. J. Surg. **68**:268-269 (May) 1945.

829. Andreasen, A. T.: Simplified Shoulder Abduction Splint, Lancet **2**: 600 (Nov. 4) 1944.

830. Phalen, G. S.: Cast-Caliper Brace for Immobilization of Hip, J. Bone & Joint Surg. **27**:724-726 (Oct.) 1945.

been obtained had he carried the body part of his short spica well over the costal border. The idea is an excellent one, however, and is the reverse of what one of us has done on many occasions; i. e., he has attached a pelvic band or a body brace to a leg plaster by uprights connecting the two. Many occasions may develop in which this unconventional combination of plaster cast and brace may be employed.

A new imbodiment of a method for preventing rotation in a brace for the cervical part of the spine when the need for actual support of the head does not exist has been published by Boldrey.[831] To a well fitting occipital plate, flanges are attached just below the lobe of the ear and extend forward around the maxillary bones to the ala of the nose. This gives the desired relief to motions of the mandible and yet prevents rotation of the head. The illustration shows the arrangement well.

Whigham [832] published the description of an ice-tong-like spring clip which for temporary Thomas splint traction to an injured leg can be quickly attached to a boot heel. He also suggests the use of a jacket sleeve as a Thomas splint sling.

In line with Bunnell's ideas relative to the value of mobilization splints, particularly for the hand, Feltner [833] has devised a reversible easily made splint for forearm, wrist and finger facilitating the type of mobile splintage desirable for injuries of the peripheral nerves. The article is well illustrated. A somewhat similar but less easily understood apparatus was described by Herzog.[834] This was devised particularly for radial nerve palsies rather than the more complicated finger involvements.

Technic.—While there is nothing in it that has not been said before, it is felt that in a review of last year's literature Darrach's [835] splendid article on "Surgical Approaches for Surgery of the Extremities" should start off this subtitle. He states that the criteria for a good surgical approach are as follows: (1) It should provide comfortable access to the structures sought for; (2) it should do as little damage as possible;

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831. Boldrey, E.: Supportive Immobilization of Cervical Spine, Surg., Gynec. & Obst. **80**:107-108 (Jan.) 1945.

832. Whigham, J. R. M.: Clip for Use with Thomas Splint, Brit. M. J. **1**:265 (Feb. 24) 1945.

833. Feltner, J. B.: Mobilizing Splints in Treatment of Motor Nerve Injuries, M. Bull. Mediterranean Theat. Op. **2**:162-166 (Dec.) 1944.

834. Herzog, E. G.: Splint for Radial Nerve Palsies, Lancet **2**:754 (Dec. 9) 1944.

835. Darrach, W.: Surgical Approaches for Surgery of Extremities, Am. J. Surg. **67**:237-262 (Feb.) 1945.

(3) it should pass between rather than through muscles; (4) it should pass these muscles opposite their blood and nerve supply; (5) it should permit actual visualization of important structures or pass a safe distance from them, and (6) it should be possible at the close of the operation to restore the disturbed structures to their normal position. He takes up particularly the shoulder, including the useful transacromial as well as the anterior and posterior approaches, the arm, the forearm, the thigh (exposing the femur) and the lower part of the leg. The importance of adequate length of incisions is stressed. Dr. Henry Marble, of Boston, in discussion stated all too truly that the length of an incision varies with the age of the surgeon.

One might say that this excellent article of Darrach's is a preface to Nicola's [836] valuable book "Atlas of Surgical Approaches to Bones and Joints." Nicola's book has nothing particularly new in it, but it unquestionably is a stimulus in the progress of our specialty, especially with our junior members. As has been stated, a large part of the success of an operation depends on an adequate approach, and a surgeon would do well to consult this publication the evening before he embarks on a surgical procedure with which he is not perfectly familiar. It is a true vademecum.

Straub, Thompson and Wilson's [837] paper on the results of epiphyseodesis and femoral shortening with the Phemister technic is of considerable importance and concern at least to the reviewer. The Phemister technic was employed in the arrest of growth, and over one fifth of the patients experienced growth deformities, only half of them severe enough, however, to justify surgical correction. The inaccuracy of any known method of predicting growth of bone was justifiably stressed. White [838] reported a series of cases in which a modification of Phemister's technic was employed consisting essentially of a deeper penetration of the cortex in the local bone grafting procedure, in which no deformities had developed. White had empirically figured on cessation of growth in girls to be at 16 years and that in boys a year later. Using this as a premise and figuring ⅜ inch (about 1 cm.) retardation would result from epiphyseodesis of the femur and ¼ (0.6 cm.) at the proximal end of the tibia, he reported satisfactory results in his series of cases. It is obvious that further work must be done on this problem, particularly as regards the age at

836. Nicola, T.: Atlas of Surgical Approaches to Bones and Joints, ed. 1, New York, The Macmillan Company, 1945.

837. Straub, L. R.; Thompson, T. C., and Wilson, P. D.: Results of Epiphyseodesis and Femoral Shortening in Relation to Equalization of Limb Length, J. Bone & Joint Surg. **27**:254-266 (April) 1945.

838. White, J. W., in discussion on Haas.[839]

which, in a given case, growth of bone can be expected to be completed. Todd's "Atlas of Bone Maturation of the Hand" is now being employed by White in ascertaining this age in individual cases.

These authors were much more satisfied with their results after femoral shortening, none of them however in patients less than 13½ years of age, the average correction being a little short (⅛ inch [0.32 cm.]) of 2 inches (5.1 cm.).

Haas [839] in another article on retardation of growth reported experiments on animals in which wire loops were used around the metaphysial plate through the diaphysis and epiphysis. He hopes to prove that by maintaining and releasing these wire loops, growth of bone can be controlled. This work is still in the experimental stage, and further reports will be made later. This research work is most important and will be followed with much interest.

Billig [840] in an article discussing gradual progressive fascial ligamentous contractures with advancing years with their sequelae, such as sciatica, advises their release by physical therapeutic means including particularly stretching exercises. This is a good conservative article to read during the fortunately gradually waning furor about disk lesions.

Flanagan [841] has devised an instrument for measuring the depth of screw holes, facilitating the use of a screw of the proper length. Any rod of smaller caliber than the smallest hole that is likely to be bored through bone, with a slight hook on the end to catch on the deep end of the bone would do, but as we rarely have such a rod, it is an instrument that should be in the bone kit of those of us that use a good many bone screws.

Supporting McKeever's favorable attitude toward the use of cellophane where union of two adjacent structures is to be avoided, as in tendon work, Harley [842] reports 3 cases in which he has used it successfully: (1) for making the tunnel for the long extensor of the index finger, (2) another for the adherence of the distal portion of the triceps to the humerus and (3) to prevent the recurrence of a synostosis between the radius and the ulna in a fracture. It is generally conceded, however, by those doing most of this work that tantalum is the interposing material of choice.

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839. Haas, S. L.: Retardation of Bone Growth by Wire Loop, J. Bone & Joint Surg. **27**:25-36 (Jan.) 1945.

840. Billig, H. E., Jr.: Release of Fascial Ligamentous Contractures in Physical Rehabilitation, Indust. Med. **14**:270-273 (April) 1945.

841. Flanagan, J. J.: Instrument for Accurate Measurement of Bone Screws, J. Bone & Joint Surg. **27**:723 (Oct.) 1945.

842. Harley, G. H., and Breck, L. W.: Cellophane in Bone and Joint Surgery, Am. J. Surg. **68**:229-231 (May) 1945.

Another technic for rapid roentgenography in the operating-room has been published in detail by Minear.[843] This allows a readable film to be produced at a temperature of 75 F. in one and three quarters minutes and in a minute less at 95 F. The dimensions of a portable light-proof box are given in this illustrated article; the technic requires only one solution. This technic to us is superior to other quick processes in which only one solution is employed.

Anderson [844] has made a contribution to the technic of ankle fusion by suggesting the removal of the malleoli, which unquestionably sometimes keep the opposing surfaces of the talus and the tibia apart. However, he employs transfixing pins with fixation rods instead of simple plaster for immobilization and apposition. The incorporating of the pins in plaster meets with Anderson's approval, although he obviously does not feel that to be necessary.

An excellent review of the uses and dangers of a tourniquet for work on the extremities has been written by McElvenny.[845] He condemns the use of any but a pneumatic tourniquet for the upper part of the arm, and believes that the Esmarch tourniquet for the leg is better than the sheet rubber bandage. It is feared that the dangers of the tourniquet have been stressed so much that few general surgeons who read this article will use it. One of us caught himself worrying about the complications cited, in a recent case in which he used a so-called Martin sheet rubber bandage for the arm.

The added interest in spinal surgery and exploratory operations on the disks is reflected in the publishing of four articles describing somewhat similar spinal retractors, two of them self retaining. The essential principle in all of them consists in the fact that they go deeper and have different arrangement at their depth for holding the tissue away from the laminas. Meyerding,[846] Shelden and Pudenz,[847] Glaser [848] and Hoen [849] are the authors. Those particularly interested are referred to the original articles.

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843. Minear, W. L.: Rapid Roentgenography in Operating Room, J. Bone & Joint Surg. **27**:157-159 (Jan.) 1945.

844. Anderson, R.: Concentric Arthrodesis of Ankle Joint: Transmalleolar Approach, J. Bone & Joint Surg. **27**:37-48 (Jan.) 1945.

845. McElvenny, R. T.: Tourniquet: Its Clinical Application, Am. J. Surg. **69**:94-106 (July) 1945.

846. Meyerding, H. W.: Retractor Designed to Facilitate Exposure in Operations on Spinal Column and Other Deep Structures, Am. J. Surg. **67**:572 (March) 1945.

847. Shelden, C. H., and Pudenz, R. H.: Improved Retractor for Hemilaminectomy, Surgery **16**:884-885 (Dec.) 1944.

848. Glaser, M. A.: Automatic Self-Retaining Laminectomy Retractor, J. Neurosurg. **2**:285-286 (July) 1945.

849. Hoen, T. I.: Special Self-Retaining Retractor for Use in Interlaminar Approach to Hernias of Intervertebral Disk, ibid. **2**:459-460 (Sept.) 1945.

A stainless steel anastomosing tube for use in repair of tendons and nerves has been devised by McKee.[850] The caliber of the tube corresponds with the size of the tendon, and the tube has stamped through it small kick-up spikes, somewhat similar to those employed in woven bandage fasteners, to hold the ends in close apposition when they are pushed into the tubes. These holes help to permit exchange of fluid within and without the tube, make suturing unnecessary and allow immediate activity. The article is well illustrated. Unfortunately, the manufacturer of the tubes is not given.

An instrument similar to a Masson[851] fascial splitter has been devised by Webster[852] for excising tendons of amputated fingers that are interfering with the function of the remaining finger tendons. This is somewhat different from the Bunnell[853] stripper, which allows its application to an intact tendon, both ends of which are attached.

An important fundamental article on the successful transplantation of epiphysial cartilage has been published by Wenger[854]; it exhibits roentgenograms proving the growth of a transplanted proximal end of a fibula employed to replace a destroyed first metatarsal in a boy 7 years old. This disproves the contention of Haas that the epiphysial cartilage plate loses its power of causing bone growth after transplantation. This particular transplant has been growing for four years, and as the patient is still growing, the eventual fate of the transplant is unknown. It is hoped that at bone maturity a final report will be made on this fundamentally important problem.

Of more interest to the oral surgeon than the orthopedic surgeon is the vitallium mandibular prosthesis reported by Winter, Lifton and McQuillan[855] but comparable in functional importance and almost in size to the vitallium proximal femur reported in 1943 by Moore and Bohlman. Here again is demonstrated the tolerance of tissue to large masses of inert metal prostheses.

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850. McKee, G. K.: Metal Anastomosis Tubes in Suture, Lancet **1**:650-660 (May 26) 1945.

851. Masson, J. C.: New Instrument For Securing Fascia Lata for Repair of Hernia, Proc. Staff Meet., Mayo Clin. **8**:529-530 (Aug. 30) 1933.

852. Webster, G. V.: Treatment of Tendons in Finger Amputations and Description of New Instrument, Surgery **17**:102-108 (Jan.) 1945.

853. Bunnell, S.: Repair of Tendons and Description of Two New Instruments, Surg., Gynec. & Obst. **26**:103-110, 1918.

854. Wenger, H. L.: Transplantation of Epiphysial Cartilage, Arch. Surg. **50**:148-151 (March) 1945.

855. Winter, L.; Lifton, J. C., and McQuillan, A. S.: Embedment of Vitallium Mandibular Prosthesis as Integral Part of Operation for Removal of Adamantinoma, Am. J. Surg. **69**:318-324 (Sept.) 1945.

XXIII. RESEARCH

Prepared by
A. R. SHANDS Jr., M.D., and MARION H. MORRIS, M.D.
WILMINGTON, DEL.

THE REPORTS on orthopedic research and related subjects for 1945 show a preponderance of articles on neuromuscular studies. The outstanding article of the thirty-four reviewed for this section is that of Bowden and Gutmann [865] on the denervation and reinnervation of human voluntary muscle. This should be read in full by every orthopedic surgeon. The sixteen articles selected for review in this section divide themselves into the following subjects and will be presented in this order: (1) neuromuscular studies, (2) muscles and blood supply, (3) healing fractures, (4) phosphatase and ossification, (5) bone growth and hormones, (6) plastics in bone surgery, and (7) vitamin D and mineralization of bone.

Neuromuscular Studies.—Bowden and Gutmann [856] have made an excellent study of the innervation, denervation and reinnervation of human muscle in material taken from patients with injuries of peripheral nerves. One hundred and forty biopsies of different muscles from 86 cases were examined. The periods of denervation observed ranged from forty-two days to thirty years.

It was found that denervation leads to progressive shrinkage and ultimate destruction of the muscle fibers with the following observations:

(*a*) Up to three years, no degeneration and no disruption has been found in the muscle fibers. However, shrinkage and increase of connective tissue in part of the muscle may be too advanced to allow recovery after reinnervation. The essential changes during this period are: progressive but unequal shrinkage of the muscle fibers, progressive depletion of the sarcoplasm of the end plate and progressive distortion of the pattern of innervation and vascularization.

(*b*) From three years onward disruptive changes occur: Shrinkage of the muscle fibers is associated with a longitudinal splitting up of their substance into individual myofibrils and with transverse fragmentation. These fragments are found embedded in connective tissue by which they are ultimately replaced. There is no indication of direct metaplasia into collagenous fibers. In the latest stages of denervation, muscle fibers may be represented by tubes filled with pyknotic nuclei and granules of irregular size and distribution or by small round or oval fragments of degenerated muscle tissue. Cross striation of muscle

856. Bowden, R. E. M., and Gutmann, E.: Denervation and Re-Innervation of Human Voluntary Muscle, Brain **67**:273-313 (Dec.) 1944.

fibers may remain intact up to the latest stages of denervation but is lost in the small fragments which may show hyaline and vacuolar degeneration of the cytoplasm. Changes in the nuclei lead to pyknosis and ultimately karyorrhexis.

(*c*) Up to three months after denervation, the pattern of innervation is intact and the individual Schwann tubes can be followed to their end plates. After about three months, the end plates become increasingly difficult to identify and the pattern of innervation is distorted progressively by the proliferating connective tissue.

(*d*) In the early stages of denervation there is apparently an increase in the permeability of the vessels leading to the formation of perivascular infiltrations. There is a progressive thickening of the walls of the vessels. The pattern of vascularization is distorted by increasing connective tissue formation. The rich anastomotic network of capillaries is reduced. Finally, the vessels may be completely blocked.

(*e*) In the latest stages of denervation muscle is represented by fat, connective tissue vessels and the larger empty nerve trunks.

(*f*) The time of denervation is not the only factor determining the degree of atrophy. There are indications that age, stretch, sepsis and other factors play some part in influencing the degree and rate of atrophy.

(*g*) The changes in the muscle may be reversed to some extent by reinnervation providing that the integrity of the muscle fibers itself is not attacked. Fragmentation is usually found after three years and represents an irreversible change. Up to three years, delay of repair influences progressively the degree of recovery; after three years the possibility of any useful recovery is in question.

Muscle biopsies were found to provide aids to diagnosis, prognosis and treatment in selected cases of peripheral nerve injuries. The criteria used to evaluate these biopsies are: (*a*) the state of the muscle (degree of atrophy), (*b*) the state of the nerve (degree of reinnervation) and (*c*) the period of reinnervation (time between biopsy and the expected arrival of nerve fibers). This is calculated on the assumption that the lesion is an axonotmesis. It is then compared with the state of the nerve and muscle found in the biopsy, and a diagnosis can then be made.

The studies showed that different types of lesions in the main nerve trunk give a characteristic pattern of reinnervation in the muscles, the degree of reinnervation depending on the nature and duration of the lesion. It is possible to distinguish between neuropraxia, partial lesions, axonotmesis and a group composed of unsuccessful sutures, traction injuries, etc. When neither empty nor innervated nerve trunks are found, a diagnosis and prognosis can be given based on the state of the muscle.

In the study there is evidence that the rate of outgrowth of the tips of axons in man is not less than 3 mm. a day after an axonotmesis.

There has been no evidence that muscle biopsy is a procedure harmful to the patient. A muscle biopsy may be performed using local anesthesia. The main indications for biopsy are: (*a*) to determine the degree of atrophy, extent of fibrosis or presence of vascular changes in a muscle when full clinical examination has failed to give conclusive evidence; (*b*) to determine the nature of the lesion of the nerve when the history and clinical examination fail to provide all the necessary data; (*c*) to determine whether a satisfactory, uniform wave of reinnervation is occurring in long-standing high lesions of nerves (the changes of reinnervation of the distal muscles and cutaneous sensory end organs may be assessed by examination of one of the more proximal members of the muscle group); (*d*) to assist in determining whether exploration, resection and resuture are indicated after a primary or secondary nerve repair; (*e*) to determine whether delay or return of functional recovery is due to the state of the nerve or muscle or both, and (*f*) to provide additional confirmation of the necessity for operation when the patient needs reassurance.

The limitations of biopsy are: (*a*) The biopsy specimen may contain no nerve trunks (out of 140 biopsy specimens 7 contained no nerve trunks; 3 contained only perivascular fibers; this represents 7.1 per cent of the total). (*b*) A biopsy is only a small sample; when the lesion is a partial one an unduly favorable or unfavorable impression may be gained. (*c*) Sufficient time must have elapsed for reinnervation to have occurred, and if the lesion is high it may not be justifiable to wait for biopsy before exploring the nerve.

Finally, the authors concluded that a repair of nerve three years or more after injury is unlikely to be followed by any useful functional recovery of the muscle.

[Ed. Note.—This article contains a tremendous volume of important data for every surgeon treating peripheral nerve injuries. The authors state that the growth of nerves is not less than 3 mm. a day; most of the teaching is 1 to 2 mm. a day. From the authors' observations, certainly three years is a sufficient length of time to wait for the regeneration of a nerve before transplantation of tendon and muscle is to be considered.]

Hines, Melville and Wehrmacher [857] studied the effect of electrical stimulation on neuromuscular regeneration and muscular atrophy.

The object of the investigation was to determine the over-all effects on neuromuscular regeneration of a regimen of electrical stimulation which had been proved to be effective in delaying denervation atrophy

857. Hines, H. M.; Melville, E. V., and Wehrmacher, W. H.: Effect of Electrical Stimulation on Neuro-Muscular Regeneration, Am. J. Physiol. **144**: 278-283 (July) 1945.

and to determine the time after denervation during which electrical treatments are most effective.

Daily faradic stimulation was effected on the gastrocnemius in an adult albino rat after tibial nerves had been crushed.

The results were as follows: 1. Daily treatments greatly retarded the loss of weight and strength in muscles prior to their reinnervation (retarded rate of atrophy). 2. Treatments had no effect on the time of onset of functional reinnervation and on normal innervated muscle. This observation indicates that electrical stimulation neither hastens nor retards the progress of axon outgrowth and its establishment of functional contacts with denervated muscle. 3. Electrical stimulation and the stretching and fatigue resulting therefrom appeared to be without injurious effects on any phase of neuromuscular regeneration. 4. When treatments were continued for some time after reinnervation, the differences between the treated nerves and muscles and their untreated contralateral controls were found to be gradually equalized. At thirty-five days after denervation there was no difference between the strength of the treated and untreated muscles and only a small difference between the weights of the muscles. The experiments in which the electrical treatments were delayed until after the onset of initial reinnervation showed comparatively little benefit from electrical stimulation. Thus an evaluation of the effects of electrical stimulation will be prejudiced by the time after denervation at which critical measurements are made.

Thus electrical stimulation by retarding muscular atrophy enables the regenerating axons to make functional contacts with larger and stronger muscle fibers.

[Ed. Note.—From the results of these experiments, it can be inferred that daily faradic stimulation of muscles following nerve injury may be indicated up to the time of the complete regeneration of the nerve.]

Van Harreveld [858] attempted to explain the hypothesis that after the removal of part of the innervation of a muscle the remaining motor units grow by "adopting" muscle fibers which originally belonged to the denervated motor units.

A severe paresis is produced in the quadriceps and sartorius muscles of rabbits by pulling the sixth lumbar nerve out of the cord. The small contingent of motor fibers from the fifth lumbar nerve forms the sole remaining motor innervation of these muscles.

Forces which developed in the right and left sartorius and quadriceps muscles during stimulation of the fifth lumbar nerve were recorded. A few months after the removal of the sixth lumbar nerve on one side, it was found that the force produced on the side operated on was consider-

858. Van Harreveld, A.: Re-Innervation of Denervated Muscle Fibers by Adjacent Functioning Motor Units, Am. J. Physiol. **144**:477-493 (Sept.) 1945.

ably larger than on the control side. This increase in muscular force starts about two weeks after removal of the sixth lumbar nerve. It is considerable during the first few months and has not quite ceased after six months.

No serious or obvious degeneration was usually found in the sartorius two months after removal of the sixth lumbar nerve, even in the instances in which this muscle was innervated originally only to a small extent by the fifth lumbar nerve (as indicated by the small forces developed on the control side during stimulation of the fifth lumbar nerve).

The average surface of the cross section of the muscle fiber in the sartorius on the side operated on was larger than on the control side.

He concluded: ". . . the increase in force observed a few months after the partial denervation of the sartorius and quadriceps muscles is due mainly to an adoption by the motor units belonging to the fifth lumbar segment, of muscle fibers innervated originally by L 6. This adoption would be made possible by an increase of the branching of the end ramification of the motor fibers of L.5. It is possible that the increase in thickness of the muscle fibers is an additional factor in the increase of muscle force of the partially denervated muscles."

[Ed. Note.—The thought contained in this paper of the adoption of paralyzed muscle fibers by normal and uninjured nerves certainly suggests that this idea may be the explanation of some of the return of muscular function in infantile paralysis as well as in obstetric paralysis. The importance of these observations is so great that the experiments should be continued and repeated by others.]

Gutmann [859] attempted a heteroinnervation of muscle with sensory nerve fibers by suturing the sural nerve and the peripheral stump of the peroneal nerve in rabbits. The effects of denervation were not arrested, and the atrophy proceeded even after the sensory nerve had entered the muscle. Stimulation of the sural nerve did not produce contraction.

The sensory nerve cannot make terminal branches or form new end plates. The endings resemble those in skin at first, being netlike. These fail to persist and disappear, and then filaments run between muscle fibers.

He concluded that only motor fibers are responsible for maintenance of "trophic" conditions and that only they are able to arrest and reverse atrophic changes of muscle fibers in rabbits.

[Ed. Note.—The negative results of these experiments are important. It will certainly clear up the subject in the minds of many physicians

859. Gutmann, E.: Reinnervation of Muscle by Sensory Nerve Fibers, J. Anat. **79**:1-8 (Jan.) 1945.

who have thought of the possibility of a sensory nerve functioning as a motor nerve.]

Eisenhauer and Key [860] attempted to determine two things: (1) the optimum position of fixation of limbs in order to conserve muscle power and (2) the best method of treatment of muscles paralyzed by loss of nerve supply. They developed a method of recording on a kymograph the twitch strength of the gastrocnemius-soleus group of muscles in cats as a criterion of disuse and denervation atrophy.

This method was applied to the study of disuse atrophy. After normal values were determined, legs were immobilized for six weeks, with the muscle group in stretched, relaxed and neutral positions. Stimulation for eight weeks following removal of the cast showed moderate and persistent disuse atrophy in muscles which were stretched, whereas the relaxed and neutral groups showed little consistent effect.

Denervated cats also were immobilized in various positions, but the study was unsatisfactory because no definite contraction plateau could be obtained in response to stimulation. However, they suggest that denervated muscle atrophies less if left alone than if immobilized. They believe that the danger of "stretch paralysis" has been overemphasized. By the same reasoning they believe that the nerve should be repaired before the bone is healed when fractures are complicated by peripheral nerve injuries.

Riley, McCleary and Johnson,[861] because of the established relationship of choline to fat and protein metabolism, were prompted to study the effect of choline on atrophy of muscle and bone. Their conclusions were: 1. Daily parenteral administration of choline chloride had no effect on the course of denervation atrophy of rats. 2. Following unilateral section of the brachial plexus, the humerus continued to gain in mass, although more slowly than normal. 3. The twenty-four hour uptake of radioactive phosphorus by bone ash is the same on the basis of ash weight in normal and atrophic limbs. 4. The phosphorus of tracer doses of calcium phosphorylcholine chloride does not enter bone ash preferentially over that of inorganic phosphate.

Muscles and Blood Supply.—Using bromphenol blue as an indication of effective vascularization of muscular tissue, Clark and Blom-

860. Eisenhauer, J., and Key, J. A.: Studies on Muscle Atrophy: Method of Recording Power in Situ and Observations on Effect of Position of Immobilization on Atrophy of Disuse and Denervation, Arch. Surg. **51**:154-163 (Oct.) 1945.

861. Riley, R. F.; McCleary, B., and Johnson, R. E.: Denervation Atrophy of Bone and Muscle: Examination of Effect of Choline and Some Further Observations on Metabolism of Phosphorylcholine and Deposition of P32 in Bone, Am. J. Physiol. **143**:677-686 (May) 1945.

field [862] studied the results of interrupting the blood supply to muscles of rabbits.

The efficiency of intramuscular anastomosis varies in different muscles. The tibialis anticus has two main arteries of supply, and ligature of the lower artery leads to devascularization of the distal half of the muscle with necrosis. Partial interruption of intramuscular vascular channels results in localized areas of devascularization.

They found that necrotic areas are rapidly replaced by regenerated muscle fibers leading to partial reconstitution of muscle.

Experimental gunshot wounds of thigh muscles in rabbits were found to give rise to circumscribed patches of devascularized areas extending some distance from the path of the missile. The importance of this observation was mentioned in connection with gunshot wounds in human beings.

In studies on regeneration of muscle, Clark [863] found that in the rabbit the lower one half or two thirds of the tibialis anticus can become completely reconstituted after undergoing ischemic necrosis.

He believes that regeneration is formed entirely as outgrowths of preexisting muscle fibers and not by differentiation of generalized connective tissue cells.

[Ed. Note.—The thought expressed in this article as well as the preceding one that muscle fibers regenerate themselves as outgrowths of preexisting muscle fibers is contrary to present teaching. It is generally accepted that in higher vertebrates new striated muscle cells cannot be formed by the division of preexisting muscle cells and that they cannot be formed from other types of cells such as fibroblasts.]

Blomfield [864] injected radio-opaque substances into the main limb vessels of a cadaver. Individual muscles and groups of muscles were then dissected out, removed and examined roentgenologically. Five types of vascular patterns were recognized: (1) a longitudinal anastomotic chain formed by a succession of separated nutrient vessels entering muscle throughout most of its length (soleus and peroneus longus); (2) a longitudinal pattern of vessels derived from a common stem and entering one end of the muscle (gastrocnemius) (one would expect this to be unusually susceptible to vascular damage); (3) a

862. Clark, W. E. L., and Blomfield, L. B.: Efficiency of Intramuscular Anastomoses, with Observations on Regeneration of Devascularized Muscle, J. Anat. **79**:15-32 (Jan.) 1945.

863. Clark, W. E. L.: Regeneration of Mammalian Striated Muscle, Nature, London **156**:109 (July 28) 1945.

864. Blomfield, L. B.: Intramuscular Vascular Patterns in Man, Proc. Roy. Soc. Med. **38**:617-618 (Sept.) 1945.

radiating pattern of collaterals arising from a single vessel entering the middle of the muscle (biceps), (4) a series of anastomotic loops throughout the length of the muscle and derived from a succession of entering vessels (tibialis anticus, extensor hallucis longus and long flexors of the leg), and (5) an open quadrilateral pattern with sparse anastomotic connections (extensor hallucis longus).

A survey of the relative vulnerability of muscles to necrosis and clostridial infections as related to vascular pattern is being made. A preliminary survey is mentioned, and the final survey is forthcoming.

[ED. NOTE.—The observations in this article certainly are most important and should aid in the determining of the extent of infection as well as necrosis after injury when muscles are involved. This should be especially true of infection and necrosis in the gastrocnemius muscle.]

Healing Fractures.—Marshak and Byron [865] present a method of studying the uptake of radiophosphorus and radiostrontium (radioactive tracers) in the healing of uniform bone lesions of rats in vivo.

They used radioactive isotopes of strontium (Sr89) and phosphorus (P32) to study the metabolism of these elements in healing bone. Radiostrontium was used instead of radiocalcium because it behaves similarly but is more convenient technically. Uniform lesions were made in the tibia of a rat. Twenty-four hours before measurements were made, the animals were given the radioactive solution (radiophosphorus as sodium acid phosphate or radiostrontium as strontium chloride) intraperitoneally. Both give off beta particles of the same energy value, and the radiations were measured by a Geiger-Müller counter. The counter was shielded by a lead plate with an aperture 2 by 5 mm. so as to register beta particles from the wound only. The counter was checked against a known standard of uranium oxide each day before use.

The results were: In young animals, the latent period for an increased uptake of phosphorus is shorter than in older animals (two compared with four days). The maximum uptake of phosphorus and strontium occurs on the eighth to tenth day in young rats, as compared with a maximum of fifteen days reached in old rats. This parallels the gross healing of the old and young bones. By comparing the ratio of uptake of strontium and phosphorus, it is seen that this ratio tends to increase later in the healing process (more phosphorus and less strontium is taken up in the early stages of healing, as compared with the later stages); it may be possible to utilize this tendency to differentiate between the proliferating and the calcifying stages of bone healing.

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865. Marshak, A., and Byron, R. L., Jr.: Method for Studying Healing of Bone, J. Bone & Joint Surg. **27**:95-104 (Jan.) 1945.

Copp and Greenberg [866] report studies on rats in which the fibula was fractured. Twenty-four hours before killing they gave radioactive strontium and then measured areas with the Geiger-Müller counter. The calcification activity was determined by the uptake of radioactive strontium by callus and compared with the opposite normal fibula.

The results were as follows:

In normal rats most active calcification was in eight to sixteen days. The broken bone attains the strength of the opposite in twelve to sixteen days. In vitamin A–deficient rats the callus was smaller and calcirats no significant calcification of callus was noted until vitamin D was added. With rats given toxic doses of vitamin D the callus was small and the calcification activity was reduced.
fication was less active with a delay in healing of the fracture. Large doses of vitamin A gave the same results as in normal rats. In rachitic

[ED. NOTE.—The results of these experiments confirm some of our present day concepts of vitamin deficiency and bone healing.]

Brush [867] gave a series of rats 0.33 mg. of thyroxin and 0.33 mg. of diethylstilbestrol three times weekly intramuscularly.

Her conclusions were: 1. Neither affects the healing process of fractured fibulas, except possibly by slight retardation, from diethylstilbestrol more than from thyroxin. This is probably nonspecific. 2. Thyroxin accelerates proliferation, differentiation and resorption of cartilage and bone at the tibial epiphysis. The width of the cartilage disk is reduced, and the number and size of trabeculae below the plate decreased. The matrix undergoes calcification and regressive changes indicative of aging. Longitudinal growth remains normal. 3. Diethylstilbestrol inhibits the proliferation and resorption of cartilage and bone at the tibial epiphysis. The subepiphyseal trabeculae are abnormally long and heavy and often contain heavy strands of calcified cartilage which have failed to undergo resorption. The animals are stunted in growth. This is similar to the effects described by other authors employing natural estrogens.

Phosphatase and Ossification.—Studies on horse and sheep embryos regarding the role of phosphatase in ossification of embryonic bone, performed by Roche and Mourgue,[868] led to the conclusion that the role of phosphatase is not to favor precipitation of tricalcium phosphate by the mechanism described by Robison but to permit accumulation of

866. Copp, D. H., and Greenberg, D. M.: Studies on Bone Fracture Healing: Effect of Vitamins A and D, J. Nutrition **29**:261-267 (April) 1945.

867. Brush, H. V.: Effects of Thyroxin and Stilbestrol on Healing of Fractures in Rat, Am. J. Anat. **76**:339-373 (May) 1945.

868. Roche, J., and Mourgue, M.: Premières étapes de l'ossification dans les os embryonnaires et role de la phosphatase, Compt. rend. Acad. d. sc. **214**:809, 1942.

phosphoric radicals in the prebony substance, which independently fixes calcium. The formation of tricalcium phosphate then takes place only after this first phase of ossification is completed. The results also suggest that one of the chief functions of the osteoblasts is the secretion of enzymes (proteases and phosphatase) participating in formation of bone.

Bone Growth and Hormones.—Estrogen and a hormone produced by the anterior lobe of the hypophysis accelerate skeletal aging in growing animals. However, the two hormones accomplish this effect in different ways. The anterior hypophysial hormone stimulates growth and hastens epiphysiodiaphysial union by inducing premature regression and resorption of the epiphysial cartilage; estrogen, on the other hand, inhibits growth and resorption, thus delaying epiphysiodiaphysial union. In view of these contrasting mechanisms, M. and R. Silberberg [869] thought it of interest to investigate the combined effects of these two hormones on skeletal development and aging. Thirty-two virgin female mice 5 to 6 weeks old were given the combined substances. Two types of controls were used, (1) untreated mice and (2) those given only one of the hormones. Results were as follows: Histologic study of the lower part of the femur and upper part of the tibia was performed. In growing mice the skeletal effects of estrogen can be modified by the simultaneous administration of an extract of the anterior lobe of the hypophysis. The two hormones oppose each other in their action on the growth of cartilage, but they cooperate in accelerating the age changes in the latter and in the overproduction of bone—anterior hypophysial hormone by stimulating osteoblastic bone formation and estrogen by promoting hyalinization of the marrow and by inhibiting the resorption of bone. (The changes in the bone represent a combination effect involving two different mechanisms: The anterior hypophysial extract stimulated osteoblastic bone formation; the simultaneously injected estrogen diminished the osteoblastic activity. But this decrease in active formation of bone was more than compensated for by the lag of resorption of the primary spicules.) Thus, the two hormones do not neutralize each other but each tends to exert its own effect on the receptor tissue. The skeletal effects of estrogen are direct ones and are not mediated by the anterior lobe of the hypophysis.

Plastics in Bone Surgery.—Blum [870] performed a series of experiments on animals in which he inserted absorbable protein plastics and

869. Silberberg, M., and Silberberg, R.: Combined Effects of Estrogen and Anterior Hypophysial Extract on Skeleton of Growing Mouse, Arch. Path. **39**: 381-387 (June) 1945.

870. Blum, G.: Experimental Observations of Use of Absorbable and Non-Absorbable Plastics in Bone Surgery, Proc. Roy. Soc. Med. **38**:169-171 (Feb.) 1945.

nonabsorbable, nonprotein plastics in bone and soft tissue. These were machined into plates, screws, nails, etc.

The protein plastics were made of (1) casein, (2) fibrin, (3) casein with plasma, (4) casein with red blood cells and (5) casein with whole blood, formalized by emersion in 4 per cent formaldehyde. These plastics had less strength than metals but about the same strength as bone. They were found to be completely absorbed in soft tissue and bone, had no harmful effects on the tissues and when inserted into bone were replaced by bone. The rate of absorption of the plastics depended on the degree of formalization, the size of the implant and the tissue into which the plastic was implanted.

The following nonprotein plastics were implanted into the same tissues: (1) methyl methacrylate, (2) cellulose acetate, (3) nylon, (4) urea formaldehyde and (5) phenol formaldehyde. These plastics were found to have no outstanding advantages over metals. The disadvantage was that they were not so strong as metals. Many of these nonprotein plastics destroyed embryonic tissue cultures, which would certainly be another disadvantage to their use. Methyl methacrylate was one of the nonprotein plastics which did not destroy embryonic tissue cultures.

[ED. NOTE.—These observations appear to be of great value to those considering the use of plastics in bone surgery. The fact that embryonic tissue cultures are destroyed by some nonprotein plastics should emphasize the need for careful study before using this type of plastic in the human body.]

Vitamin D and the Mineralization of Bone.—Greenberg [871] reports a series of experiments on rachitic rats to determine the effect of vitamin D. He has conclusively shown that vitamin D exerts a direct effect on the mineralization of bone in these rachitic animals as well as promoting the absorption of calcium from the digestive tract.

Young weaned rats were fed rachitogenic diet (Steenbock-Black) for fifteen to twenty days. At the end of this period all the rats had become rachitic. Some of these rachitic rats were now given vitamin D in the form of irradiated ergosterol seventy-two hours before the administration of radioactive calcium (Ca45) and radioactive strontium (Sr89). The control rachitic rats were not given the irradiated ergosterol before the administration of the radioactive substances.

The results showed that the excreta and skeleton contained the bulk of the radioactive substances, the amount in the soft tissue being

871. Greenberg, D. M.: Studies in Mineral Metabolism with Aid of Artificial Radioactive Isotopes: Tracer Experiments with Radioactive Calcium and Strontium on Mechanism of Vitamin D Action in Rachitic Rats, J. Biol. Chem. **157**: 99-104 (Jan.) 1945.

negligible. In the rats treated with vitamin D about 15 per cent of the radioactive calcium and 30 per cent of the radioactive strontium passed through the intestinal tract unabsorbed, while in the nontreated group 40 per cent of the calcium and 45 per cent of the strontium passed through unabsorbed. The bones of the rats treated with vitamin D retained a larger proportion of the calcium and strontium than the bones of the rats not treated with vitamin D. Furthermore, the rats recovering from the effects of rickets accumulated nearly twice as much radioactive calcium and strontium per gram of dry bone and one and one-half times as much radioactive calcium and strontium per gram of bone ash as did the rats not recovering from rickets.

[Ed. Note.—From these observations, it appears that in diseases and other conditions showing atrophy of bone vitamin D therapy may be indicated if it is desirable either to increase the mineralization or to prevent the demineralization of bone.]

PREFACE

IN THE preparation of this review of orthopedic surgery for 1945 the titles of 1,325 articles of orthopedic interest were selected from the *Quarterly Cumulative Index Medicus* for 1945.

The number of articles reviewed and presented in this year's "Progress" is approximately 890. This is a larger number of articles than that selected for 1944. The increase in the number of articles over 1944 is thought to be due to the number of reports from the general hospitals of the armed services and adequate time for study and writing since the return to civilian practice of those men discharged from the armed services. As in the past, each editor has selected the articles for his section which he thinks represent the most progress and have the greatest scientific interest. The chairman of the editorial board has reviewed the material prepared for each section and has made certain additions and changes which seemed indicated to standardize the publications.

Because of the delay of the publishing of the *Cumulative Index Medicus* for 1945, the reviews have been slow in being returned to the chairman of the editorial board and, as was true in the past three years, it was found impossible to send the whole "Progress" to the ARCHIVES at one time. This has necessitated a slight change in the order of publication of the sections. The preface could not be written until all sections had been submitted. In spite of the difficulties encountered in getting reprints, it is hoped that the quality of the reviews is up to standard and that the publication will prove as valuable to its readers as the "Progress" of previous years.

The members of the editorial board wish to thank again those physicians not members of the American Academy of Orthopaedic Surgeons who have rendered such valuable assistance in the preparation of the material for the various sections.

Special thanks are rendered to Dr. J. A. Toomey, of Cleveland, for editing the research portion of the section on "Poliomyelitis" and to Dr. Robert L. Bennett, of Warm Springs, Ga., for editing the physical therapy portion of the section on "Poliomyelitis."

The following physicians acted as assistants to members of the editorial board:

Dr. Ghormley: Dr. Mark B. Coventry, Dr. Cameron Allen, Dr. Robert B. Elliott, Dr. Alfred E. Jackson, Dr. Einer W. Johnson, Dr. Jack Paschall and Dr. Arnulf R. Pils.

Dr. Hauser: Dr. Robert P. Montgomery.

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Dr. Alan DeForrest Smith: Dr. L. Miller, Dr. Strassburger, Dr. J. Miller, Dr. Ralston, Dr. Blunden, Dr. Knocks, Dr. Hollins, Dr. Garber, Dr. Bush and Dr. Earp.

Both style and editorial comments have again been left to the discretion of the editors except for a few changes made by the chairman. It should be stated again, however, as in the preface of the "Progress" of previous years: "If the reader or author of any article does not agree with the editorial comment, the editorial board hopes that he will think of the remark as only one man's impression and as in no way representing the opinion of the entire editorial board or of the American Academy of Orthopaedic Surgeons.

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